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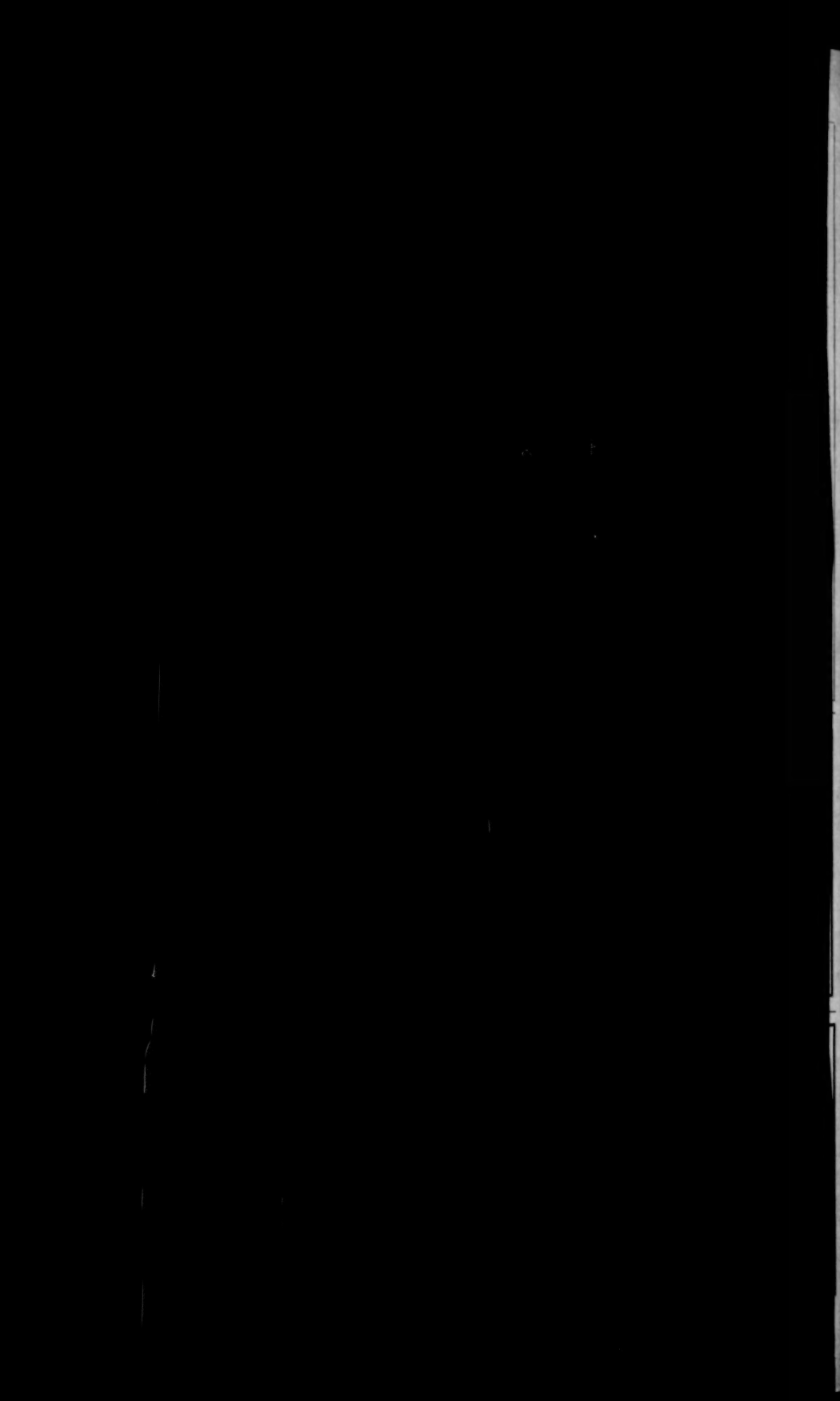

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HEREDITY IN SCHIZOPHRENIA

KAREL PLANANSKY, M.D., PH.D.

The study of heredity in the psychoses cannot be separated from the study of their etiology. If schizophrenia is a hereditary disease, we know that it can develop only in persons who possess a specific gene, transmitted to them by their parents. Obviously, a genic determination does not cover the whole of the pathogenesis. Even if the basic genic determination is established, we still have to investigate other co-determinative agents. In this manner we shall study deviant behavior as another instance of human variation.

The importance of heredity in psychoses is not a matter of conviction or of a declared adherence to a certain school of thought. It is a matter of evidence, as in any other biological study. It is the aim of this article to present a brief review of the observations and thoughts of the investigators who, during the past four decades, have been assembling and interpreting evidence regarding the role of the genes in schizophrenia.

HEREDITY VERSUS ENVIRONMENT?

It is felt that the significance of environment in hereditary diseases should be clarified first because it has become a popular belief that in psychiatry, heredity excludes environment. That, of course, is incorrect. Surely, in papers dealing with genetics of the psychoses often one finds the preponderant stress on the evidence of the genetic effect, whereas only a fleeting mention may be made of the effects of environment. This emphasis is inherent in the techniques of analysis which concentrate on one variable only.

The assertion that schizophrenia develops only in persons who carry the specific genotype needs elaboration: not all individuals who are assumed to possess the specific genotype develop the psychosis. Identical twins offer the best illustration. About 25 per cent of the identical twin-partners of schizophrenic patients do not become psychotic although their heredity is the same. This fact is the simplest evidence that heredity is not the whole story in the pathogenesis.

The genes determine the structural development and the pattern of physiological functions throughout life, and they do so in a complex and constant interaction with environment. Thus, a genetic study would be incomplete without investigation of the non-genic factors. Success in recognizing the relative contributions of the genotype and environment depends largely on accessibility of the variables to analysis. It can be anticipated that the study of deviant behavior will encounter different technical problems from the study of diseases due exclusively to tissue pathology.

There are various types and degrees of interaction between specific genotypes and environment. It will be readily seen for instance that a gene determining brachydactyly is not very dependent on the external environment. Yet it must be dependent on the other genes of the developing embryo, i.e., on the genic environment. Since in most instances individuals inheriting this gene develop short fingers, we may assume this gene requires for its function such genic and external environment as is compatible with the viability of the embryo. In other words, we are unable to identify the environmental requirements of this gene more precisely than as those which are required for developmental completion of the embryo.

Obviously much more complex types of interaction between genotype and environment underlie, for instance, development of

degenerative cardiovascular disease. Admittedly, the role of heredity in this condition is obscure although it is believed that genotype is of some importance. Clinical experience indicates that sex, age, bodily type, diet and life stresses are significant factors. Even if the development of certain clinical types of arteriosclerosis could not occur without a metabolic disorder of a simple genic determination, the development of the actual disease would still depend on many intricate constellations of the genic and external environment.

These two examples illustrate extremes of the genotype-environment relationship. One can visualize a wide range representing various degrees of interaction between these two extremes. One may cite Tay-Sachs disease as an example of a neuropsychiatric condition developing apparently without specialized requirement on environment. In contrast, hysterical personality could hardy be interpreted in terms of specific genotype. Although heredity may play a certain role in personality integration, environmental experiences would probably be assigned a preponderant role by most students.

One certainly could find within this wide range the type of genotype-environment relationship that would allow for development of deviant behavior in an entirely normal environment. Such genotype-environment relationship is, in fact, genetically no less understaandable than a relationship permitting development of abnormal behavior without bad heredity. In a very simplified manner, one could visualize the variation range as representing a continuous series of graded, complementary relationships between heredity and environment. An instructive example is reported by Slater (40) who analyzed the relationship between heredity and external influences on soldiers with psychoneurotic complaints and found a significant negative correlation: the poorer the heredity in an individual, the less stress was required to upset the balance of ajustment. In contrast, soldiers with good hereditary endowment were able to sustain very severe stresses before breaking down.

A priori, genetic theory does not rule out any genotype-environment constellation as a possible underlying mechanism in psychoses. The latter must be derived from testing of observational data for agreement with the most likely hypotheses of inheritance. Obviously, the selection of the likely hereditary modes shall depend on the prevailing views of etiology and pathogenesis of the psychosis. Those who see in schizophrenia a reaction type arising from a variety of constitutional and environmental situations would anticipate several different modes of interaction between genotype and environment. Investigators adhering to the unitary concept of psychosis determined by a specific organic disorder usually postulate a strong genotype which is liable to assert itself in virtually any environment. Generally, environment must play a considerable role in pathogenesis of schizophrenia, as can be seen for instance, from the variable onset of the overt illness alone. A precise statement of the type of nature-nurture relationship in this instance would be premature.

Furthermore, it should be understood that the outwardly perceptible trait (phenotype) ensuing from the interaction of genes and environment does not represent simply a sum of separate effects, environmental and hereditary. The interaction is a more complex process than mere summation. The indices, obtained by a simplified manipulation of numerical values, assumedly representing heredity or environment, have little meaning, at least when dealing with deviant behavior.

The estimating of the relative contribution of external influences is difficult because, in addition to the uncertainty as to specificity of the genotypes, we do not know how specific the external stress must be in order to give rise to a certain form of deviant behavior. We do not know if the specific genes require a specific or nearly specific impulse with which to react in order to produce a psychotic response or other form of aberration. Does any untoward episode during the critical period of development evoke schizophrenic reaction in a person who is genotypically sensitized, or does gene-determined susceptibility act as a rigid matrix, reacting only to definite insults? Technically, only the more conspicuous differences in life histories of patients lend themselves to observation and report, and only modest conclusions can be justified concerning the alleged precipitating circumstances. Some hints might

be derived from observations on psychoneuroses. Brown (6), for example, believes that psychoneurotic reactions tend to "breed true". Analysis of external influences has not been attempted in his paper; however, one may assume that the environmental insults were about equally represented in his three groups, denoted as hysterical, obsessional and anxiety reactions. Batchelor (3) states that thwarted aggress on ensues in different forms of deviant behavior according to the individual's constitution. It may lead to suicide in some people, whereas, in individuals differently constituted it may give rise to a psychoneurotic reaction or to a psychosis. Such formulations need to be further elaborated. On the whole, environment lends itself to investigation only as an aggregate of influences which presently are largely inaccessible to differentiation.

It is to be kept in mind that the environment to which man is exposed in his critical formative period of life, and to which he is evolutionally adjusted, is not controlled experimentally, neither is it of the type of wild environment to which other species have to adapt themselves. It is largely a man-made environment, encompassing all the advantages as well as stresses of the cultural and moral habits and codes to which people interact in their respective national units and economic strata, down to the micro-environment of the narrowest social setting, family or vocation. This observation, of course, is commonplace. However, it must be kept in mind if only to point out that methods useful in zoology are in fact inadequate for dealing with human environment when deviant behavior is being studied. Psychological sensitizations derived from contacts with other close people are obviously significant yet so far have escaped assessment in genetic studies. Purely psychogenic mechanisms originally developed in interaction with environment as well as mental representations take on the significance of true external influences in subsequent life situations. Unconscious material may be legitimately considered an external agent. However, when dealing with inner conflicts, oddities of personality traits, or peculiarities of adjustment, one should watch for the ever present problem in the study of deviant behavior, namely, the discovery of determinants, apparent or probable, that give rise to the presenting symptoms of the disorder. Grave errors are frequently introduced into the study of the nature-nurture interaction by confusing early signs of the disease for its cause.

To sum up the discussion on the place of environment in hereditary psychiatric disorders, one should emphasize that the proper position is not that of "heredity versus environment". Rather, one should formulate inquiry in terms of the relative weight of the genotype and of the environment, respectively, in determining the particular clinical category and individual instance of deviant behavior.

Furthermore, from the genetic viewpoint, one cannot accept psychotic reaction as a fixed congenital aberration, or a self-limited error in homeostasis, or merely an unfortunate episode in adjustment. Genetically, a psychosis has to be viewed as a continuous process in the biological history of the person. Simply ascertaining the presence or absence of psychosis in members of a family for the purposes of statistical analysis is apt to bring forth only partial information on outwardly observable characteristics of lives whose biological uniqueness remains unknown. The study of heredity and environment in human lives is facilitated by a dynamic concept of constitution, based on genic endowment. Continuous adaptive changes take place as new, genetically determined functions in their appropriate time enter into the individual's physiology, in order to fulfill life according to the image of the species in the prevailing environment. The cumulative effect of adaptive responses to environment, in effect, becomes incorporated into constitutional potentialities. The dividing line between heredity and external agents becomes more and more blurred as the individual grows older. Time may, therefore, be viewed as the third dimension of the constitution. The ontogenic task of the genotype is bound up with time. The type and degree of genic interaction with environment change with time and thus always new and different genotype-environment relationships crop up throughout the individual's life history. Finally, the relative influence of heredity and environment in the causation of the psychotic process may vary at different points in the

individual's life. In this connection, it is of interest to note that Anastasi (2) recommends more attention to organic versus experiential influences rather than to heredity as against environment.

From this brief discussion it can be seen that very definite, simplifying statements concerning the relative contributions of heredity and environment in the genesis of a psychosis cannot be substantiated either by clinical evidence or by genetic hypothesis. In fact, the interaction of genes with environment still represents the most difficult and least explored field of general genetics.

Which Types of Heredity May Operate in Genesis of Deviant Behavior?

In the earlier phase of genetic investigations in psychiatry only one type of heredity was considered, namely hereditary transmission mediated by genes of major effect. This term connotes a gene which determines a trait clearly discernible from the trait, caused by its allele. (The later is the gene occupying the same locus on the homologous chromosome; the alleles can mutate one to another.) In other words, the gene of major effect is the classical Mendelian gene. Its effect is assumed to be large in relation to other genes or, more precisely, to the rest of the individual's variation. Needless to say, every trait is determined actually by all the genes of the individual. However, operationally we have to select one pair of genes (alleles) from the whole of the individual's genotype in order to follow the transmission of differences of a single trait through generations. In this connection the classical Mendelian gene is also called main gene. It could be visualized as a factor which turns the genic balance toward the studied trait.

Depending on the effective dose of the gene, hereditary transmission of major qualitative differences is conventionally divided into two modes: dominant and recessive. In dominant heredity, the presence of the gene is revealed when it is present only in single dose, that is, when it has been inherited from one parent only. In recessive heredity, the gene must be present in double dose. It must be inherited from both parents to show its effect. Parents do not show the trait if they possess the gene which they are transmitting in single dose only (which is the most common occurrence). As examples of neuropsychiatric disorders inherited through a single major gene mechanism may be quoted phenylpyruvic oligophrenia and Huntington's chorea. In the majority of inherited human diseases for which a satisfactory formal explanation of heredity is available, a major gene type of inheritance plays the significant role. These are disease entities which behave in the pedigrees according to the Mendelian rules and give the familiar 3:1 and 1:1 ratios in sibships. Evidently the great majority of heritable human pathology does not show the clear-cut differences that could be interpreted in terms of plain allelic differences.

If schizophrenia were simply a behavioral expression of a specific and clearly delineated somatic disorder, it would be logical to assume a main gene effect. In fact, most if not all of the genetically minded psychiatrists have worked on the assumption of an organic etiology, and a single gene or at least a major gene type of inheritance has been taken for granted by most investigators. However, a clear-cut allelic difference can be assumed only if the studied trait represents a well-circumscribed disease entity. Evidently, this minimal requirement does not apply to all instances of deviant behavior wherein schizophrenic reaction may or may not be accepted as proper diagnosis.

As mentioned above, the individual possessing the specific gene may not show the expected trait caused by the gene in question. The percentage of individuals showing their specific genes phenotypically (i.e., through the trait caused by genes) is in some conditions fairly constant. This phenomenon is called penetrance. Essentially, it is akin to recessivity since in both instances we are unable to perceive the effect of genes which must be present in the individual and which are manifested in other individuals.

Penetrance is, of course, considered when data are tested for agreement with a certain genetic hypothesis, and discrepancy between expected and observed incidence of the trait may be reasonably explained by lowered manifestation. If lowered penetrance is to be accepted as a valid explanation, its degree has

to be verified also by further analyses. Evidently, almost any hypothetical mode of heredity could be accommodated to a set of observational data with some manipulation of penetrance percentages. Neel (28) thinks that in the study of relatively common human traits a postulate of a penetrance lowered to 60–70 per cent or less is of dubious value. In the history of attempts to interpret the data on familial concentration of schizophrenia in terms of simple Mendelian heredity many figures of lowered penetrance were suggested, some of them of 20 per cent or even less. It is not surprising that they fit well into the proposed schema; they were introduced just for that purpose.

The modifying influence of the genic background (environment, milieu) upon the main gene is very often employed in genetic interpretations of schizophrenia. Undoubtedly, the remaining genes cannot be without influence upon the effect of the main gene selected for the study. Usually, genic background is employed in the form of somatic constitution in the customary clinical usage. For instance, degrees of resistance or susceptibility to the psychosis are explained in terms of certain somatic types, which are supposed to modify the effect of the main specific genes. Irrespective of the clinical validity of such empirical observations, the genetic mechanisms which are invoked do not lend themselves to testing. Thus, such auxiliary hypotheses, although at times attractive from the clinical viewpoint, represent only stimulating speculations.

In dealing with quantitative differences between individuals the major gene mechanisms (determining heredity of clear-cut qualitative differences) cannot be anticipated. Experimental genetics has clarified heredity of continuously distributed, measurable traits in terms of polygenes. These are groups of genes supposedly of small and similar effect, and in most simple application can be visualized as exercising additive effect. In experimental plants and animals these genes have been proven to govern (together with environment) normal structural or functional characteristics. The ensuing variation in sibs is represented by a normal, continuous frequency distribution. The effect of individual polygenes is too slight to be identified in the phenotype. This type of heredity has been suggested for measurable human traits, such as stature, weight, etc.; however, their actual operation has not been established.

In genetic interpretation of deviant behavior we are also faced with the task of finding an appropriate mechanism for continously graded traits. Many psychologists believe that personality traits can be quantitatively arranged and measured, being parts of a continuum, instead of being expressed in the usual dichotomies. When this concept is applied, individuals possessing such traits can be arranged into the usual curve representing a normal distribution of frequencies. This distribution furthermore indicates that the quantitative traits in individual instances must be determined by both the innate factors and external influences. Personality traits, that are considered socially pathological, would be simply extreme variations of commonplace characteristics.

The concept of a continuum in personality traits is most important for further genetic study of deviant behavior, including the psychoses. Obviously, this concept would suggest itself for interpretation of psychoneurotic reactions. However, the matter is not yet entirely clarified clinically. Indications that independent, unitary "neurotic" factors may be operative have been advanced, e.g., by Brown (6), Eysenck (9), and Haskell (12). Even if one accepts the theory of major gene causation of schizophrenia, one still has to account for personality traits of the individual as they are molded in their inevitable interaction with the specific psychotic process.

It would seem doubtful whether the effect of true polygenes could ever be identified in the study of personality traits. Psychologically, it is difficult to study arbitrarily-defined personality traits separated from the whole of the personality. Genetically, many varied factors contribute to the determination of such vaguely defined phenotype as is personality pattern.

Furthermore, it should be pointed out that only in a small proportion of human traits, in which there is some indication of heritability, is a satisfactory or at least tentative formal interpretation available. In some of the conditions, wherein a definite mode of heredity could

not be established, it is believed that heritability is conditioned by several qualitatively different components. Some of the common diseases belong in this category. For instance, in tuberculosis, a single major gene difference had originally been suggested as the decisive hereditary factor. However, it became clear that in a chronic infectious disease the effects of various factors in resistance must significantly influence the pattern of phenotypic distribution in sibships. Thus, the effect of the main gene, if any, might not be recognizable. Animal experimentation has shown that certain components of resistance to tuberculosis are genetically conditioned, and their characteristics indicate that different types of heredity are involved. Genetic study of human tuberculosis has brought forth observations that can be interpreted as consistent with experimental data on resistance (33).

We should accept the fact that not in every human disease for which there is an indication of heritability is a closer identification of the genic mechanism practicable. Historically, it can be understood that the first workers in psychiatric genetics tended to postulate a definite and simple Mendelian heredity for schizophrenia. However, subsequent genetic studies of human pathology have revealed that essentially only rare conditions follow the simple rules of Mendelian transmission. It will be shown in this review that the evidence for a single gene inheritance of schizophrenia is not conclusive. Alternate genetic hypotheses have not been explored.

Evidence of Heredity; Methods of Investigation

Schizophrenia is relatively a common disease, and thus the methods which proved to be useful in the study of rare diseases, permitting the testing of definite modes of inheritance, cannot be applied. Proof of heredity in psychiatric conditions has been traditionally looked for through two approaches: 1) Comparing the expectancy rates of the psychosis among the relatives of the patient with that in general population. This method was devised and elaborated by Rüdin's school in Munich and is still widely used by Scandinavian students. 2) Comparing the concordance rates of identical and fraternal twin pairs. This method has been introduced into the study of psychoses by Luxenburger (22) and in this country has been applied on a large scale by Kallmann (17). Neither of these methods is fully satisfactory and neither of them can be considered equivalent to the observations of experimental genetics.

The rationale of the first method is quite simple. An increased incidence of the psychosis in close relatives of a sample of patients (who are called in this connection probands propositi or index cases) is taken as evidence that a genetic factor is operative in the causation of the psychosis. Needless to say, exogenous factors, possibly related to familial concentration, have to be excluded first; for instance, familial concentration in endemic goiter, by itself, could not be interpreted in genetic terms.

The incidence of schizophrenia in the general population has been estimated in various European countries by many authors employing different statistical techniques. The most generally accepted estimate is about one per cent. It is calculated in the form of risk or expectancy rate. In computing the expectancy rates it is necesary to allow for the variable period in the individual's life during which schizophrenia first occurs (called manifestation, risk or danger period). The most popular procedure is Weinberg's shorter method. This method assumes that the individuals within the age limits of the risk period (15–45 usually for schizophrenia) have a progressively diminishing chance to develop the psychosis. After the risk period, for statistical purposes, the chance for those who had remained unaffected is considered nil. Thus, in calculating the expectancy the numbers of unaffected persons have to be reduced in the following manner: all persons younger than the lower limit are discarded; only half of those within the limits are taken in calculation; all persons of an age above the upper limit of the risk period are included. The resulting value is an expectancy rate which is the likelihood of developing the disease and not the direct occurrence or prevalence figure. Thus, an expectancy rate (or morbidity risk) of 0.85 per cent means that out of 100,000 newborn, 850 individuals are likely to develop schizophrenia at some point during their lifetime, providing they live through the whole of the risk period. If we

followed such a cohort of 100,000 newborn to the age of 46, we would not find 850 schizophrenics among them. The actual number would depend on all mortality within the cohort.

The estimates of familial concentration vary with different authors. On the whole, for the sibs of schizophrenics the values are around 10 per cent, for their parents about 5–10 per cent, and for their children 10–15 per cent. The actual figures calculated by various investigators, although often hotly disputed, are of less importance than their general order of magnitude as compared with values for the general population. The significance of this difference has been recently reviewed by Penrose (31). He feels that when the difference is found to be tenfold or greater, the probability of genetic causation can be considered high even in data compiled with little attention to details. This statement is stressed here because it is quite important for the argument of the present review. It applies even though various sources of imperfection can be found in the reports of individual investigators. At times fairly obvious sources of bias are encountered in the tabulated data and may have influenced the precise conclusions drawn. Yet when the accumulated evidence is reviewed as a whole, and the technical flaws are measured against the basic merits of the investigations, it becomes clear that a significant familial concentration may be taken as a basis for further work.

In order to understand the technical difficulties and the occasional lack of the conceptual clarity we must briefly review the history of modern investigations of heredity in psychiatry. Even in the pre-Mendelian period many writers endeavored to confirm the commonplace notion that psychoses "run in families". The earlier studies are valueless, not so much for lack of Mendelian orientation, but because they tended to report only interesting family cases, loaded with what was considered heredity, to prove the point. The necessity of studying large and unselected samples was recognized first by Rüdin (34). Some years later Kattentidt (18) on Rüdin's initiative introduced the method of comparison with a specially obtained general sample. The definition and selection of a good normal sample were even more difficult in his time than they are today, so that it is not surprising that the normal samples of the Munich school were generally small and not entirely devoid of selective impurities. Strömgren (44) in a review of genetic psychiatric surveys commented that the principles of their sampling were sound enough but were used in ways which gave quite unreliable results, and that the confidence in the percentages computed by the authors depended on not calculating the mean error. The latter criticism can be verified even on a casual examination of the tables.

Better population samples and better methods of assessment have recently been employed by Scandinavian workers. Their observations corroborate the magnitude of the difference between familial concentration and incidence in general population. Although several of the Scandinavian investigations deal with populations of unusual demographic characteristics (inbreeding, etc.), other surveys may serve as very useful psychiatric base-lines that yield information of wider validity (e.g., Strömgren (43), Fremming (11), Larsson and Sjögren (19)). It seems likely that further studies will simply confirm what has already been discovered.

Expectancy rates for individual diagnostic categories of psychoses include all types without respect to possible etiologic diversity. Their use for computations of definite modes of inheritance assumes that all cases are of genetic origin, and, furthermore, that each psychosis is genetically homogeneous. Neither of these assumptions has been substantiated. The expectancy rates have been used in genetic family counseling, and in this connection the term "empirical genetic prognosis" has been introduced by German workers. This term would be justified if the expectancy rates were based on genetic cases only. Furthermore, since the rates may be a composite expression of various hereditary modes, the prognostic value in individual instances would be limited. The empirical expectancy rates by themselves do not give information about the causes of psychoses. Yet so much trust had been put into those figures that, at one time and another, they have been offered and presumably used as a basis for eugenic sterilization laws.

The findings on familial concentration of psychoses (and especially of schizophrenia, since most of the pertaining work has been done on this major psychosis) can be summarized as follows: the reported excess of the studied psychosis in close relatives of psychotic probands is an indication of certain degree of genetic predisposition even if the expectancy rates are the result of several modes of heredity, and even if some proportion of the cases is independent of .any specific genic determination.

Twin Studies

Twin studies are frequently represented as a substitute for experimental manipulations of genetic and environmental factors. Identical (monozygotic) twins have identical genotypes so that all intra-pair differences must be caused by environment. In fraternal (dizygotic) twins the genotypes are different, and thus intra-pair differences are attributed to heredity and environment. It is generally assumed that their environment is as similar as that of identical twins if they live together during their formative years. Psychiatric twin studies have been used mainly to compare the occurrence of psychoses in the two categories of twins. When a psychosis is found to occur in both twin partners more frequently among identical pairs than among fraternal pairs, and external conditions are similar, the determinative role of the genotype is deemed significant. Another use of twins is in the comparison of developmental histories of individual twin partners in order to elucidate the role of heredity and environment in pathogenesis.

In psychiatric studies with large twin samples it is usually assumed, for the sake of technical simplicity, that the only significant environmental variable is the gross external environment, as evidenced by the customary division of the material into two groups: pairs who lived together and pairs whose members were raised separately. It should be kept in mind, however, that there are sources of variation which influence both the genotype and the particular environment of individual identical pairs, and which are not accessible to a differentiation by the customary statistical methods. For example, there are circumstances of fetal development that make for somatic dissimilarities. Furthermore, individual patients (probands) and their co-twins in the sample are all identical as to the specific genes (provided the disease is genetically one entity), but each pair must differ from all others in the rest of the genes, that is, in the modifying genes. Thus, the differences between the various twin pairs within a sample of affected monozygotic pairs could not be attributed to the external influences to the same extent in all pairs. Hence, part of inter-pair variance seen, for instance, in concordance or discordance as to the presence of the psychosis or in its clinical modifications is caused by inter-pair differences of the genic milieu (modifiers). In consequence the percentage of concordance gives average results and does not describe in any simple way the relative effects of the specific genes and of the environment. Where the primary aim is the establishing of comparative concordance rates, environment is assumed to be nearly identical for twins who live together. However, environmental similarities within pairs are probably not as consistent as these studies usually assume. For example, unobserved episodes in the early period may cause considerable divergence of psychogenic sensitization between identical twins, leading to different behavior in later life. On the other hand, it can be assumed that interpersonal relationships of identical twins are slanted by their self-appreciation which is distinctly different from that commonly found in fraternal twins. Thus, the same family environment would be subjectively different to identical and fraternal twins.

Since the twin study in psychology has been offered almost as an experimental tool for investigation operating with a controlled environment, there has been a persistent clamor for observations on monozygotic twins who have been reared in different homes. This demand would be certainly in keeping with the experimental design. Unfortunately, a psychiatric twin study is not a study in controlled environment because the environments in twin surveys have all been decidedly "wild" environments of common human ecology. Furthermore, when it comes to a psychosis, one has to admit that there is lack of knowledge as to what variables should be controlled.

At best, one studies the life histories and gross external circumstances of twins who lived in different places and with different people. Even if one of them became schizophrenic and the other remained non-psychotic, one would not know the cause of the difference. Surely, if sizeable samples were compared as to concordance, one would learn more about the relative strength of specific genotypes. Unfortunately, twins separated early in life are extremely scarce.

The concept of concordance versus discordance has been elaborated and incorporated into a system of genetic argumentation regarding somatic traits that usually appear congenitally. Psychological traits, with the possible exception of intelligence, do not belong in this category; nor do psychotic reactions that may or may not develop during a particular period of life. Therefore, the same technical problem which is met in sibships, namely, the computation of expectancy rates with an allowance for the risk period, has to be solved in calculating concordance rates. The traditional methods, like Weinberg's "shorter method", have been used in certain reports. However, Weinberg's method was devised for estimating risk probability within groups of relatives as they occur in a population sample, but not for estimating manifestation probability within genetically identical pairs. Slater (42) found that this traditional method yielded (in his sample) figures which had little meaning. In his estimate of concordance rates he operated with attributes which he found useful in his sample of twins. These took into account the intra-pair correlation in age of onset (of the psychosis) between the twins as well as the length of time they remained well before or after illness in the proband.

Biological Unity in Schizophrenia and Specificity of the Schizophrenic Genotype

A basic difficulty in testing various hypotheses of inheritance against the empirical risk rates stems from uncertainty as to the homogeneity of the schizophrenic syndrome. Whether schizophrenia is a disease entity with single underlying genotype, or whether the apparent unity is simply phenotypic, actually concealing various genetic diseases, has always been a subject of dispute among geneticists.

The idea of genic specificity and unity was probably derived from the concept of an independent, separate and single cause for each disease entity. The simplicity of single factor, specific inheritance was very attractive to early students who were discovering Mendelism. Moreover, certain initial examples in human genetics could be demonstrated. The statistical analyses of the "empirical genetic prognosis" period were designed to confirm a single, unitary, specific factor mechanism. Individual endogenous psychoses were assigned distinct and independent loci both in the nosographic system and in the chromosomes. It was logical to explain the Kraepelian dichotomy on the basis of two distinct Mendelian units only.

Historically, the Munich school, inaugurated by Rüdin, adhered to strict specificity and unity of the schizophrenic genotype and correspondingly postulated a comparable independent unitary genotype for manic-depressive illness. At the other extreme were those who believed in splitting schizophrenia clinically into numerous semi-independent units, and (having decided upon the clinical independence of the disease subgroups) postulated, in turn, independent genotypes for each clinical subgroup.

The purity of the schizophrenic genotype has been most often tested by examining the incidence of psychoses other than schizophrenia among the relatives of schiozphrenic patients.

Rüdin (34) noted the rare occurrence and indeed the almost complete absence of manic-depressive psychosis among the descendants of schizophrenic patients. This circumstanec he deemed the more remarkable since in the parents of schizophrenics, manic-depressive psychosis was often recorded. Considering the early date at which these investigations took place, one could explain Rüdin's findings in terms of the diagnostic criteria then prevailing. Rüdin believed that the occurrence of other psychoses among the parents and siblings of schizophrenics is not accidental. He thought that they are, in some measure, closely connected with the substance and the genetic basis of schizophrenia. He visualized

the non-schizophrenic disorders of the parents and schizophrenia in their children as produced by a complex Mendelian segregation. Furthermore, he felt (35) that the schizophrenic process "mobilizes the anlage" for the manic-depressive psychosis. One senses here a residual of the ancient concept of polymorphous heredo-degeneration, characterized by interchangeable syndromes.

Penrose (30), using extensive data from the Ontario mental hospitals, observed that schizophrenia and the affective psychoses are not clearly distinct entities in terms of familial occurrence, and that the same family often includes both diagnoses.

Slater (39) speculates on alleged genotypic overlapping of schizoid traits with other mental disorders and suggests that this overlap might be accounted for by an easier manifestation in a genic milieu which includes other factors predisposing to a psychic disorder. He finds it easy to suggest that the presence of the manic depressive gene may impart to the schizophrenic gene a sort of dominance so that the latter gene can manifest itself in a heterozygous state (that is in single dose instead of a double dose). This speculation introduces a discussion of atypical psychoses half way between manic-depressive psychosis and schizophrenia. One recalls Rüdin's suggestion of schizophrenia serving to activate a manic depressive genotype. In his twin study (42), Slater found that affective illnesses among relatives of schizophrenics are seen as involutional depression. At the same time, affective illnesses in such families frequently exhibit schizophrenic symptoms. He infers that schizophrenia appearing in later life can take the form of an involutional or atypical depression. Other investigators have made similar observations.

Luxenburger (25), representing the Munich school, was convinced that the clinical subtypes in schizophrenia are not independent genetically. Rather, they should be viewed as phenotypes, resulting from a single genotype that varies widely. He asserted categorically that one must accept a single genotype for schizophrenia: "There is no evidence against it from the psychiatric viewpoint." Schulz (36) attempted to clarify the problem of genetic homogeneity by comparing the expectancy rates obtained in sibships with two or more probands with those found in all sibships. Although this examination indicated some difference and, thus, a lack of homogeneity, Schulz did not regard the results conclusive. Kallmann (14) also believes that the specific genotype is unitary; in fact, he postulates one specific allele in double dose as the determinant of all forms of the disease. However, he found that the expectation of schizophrenia is about twice as high for the children of patients in hebephrenic and catatonic groups (20.7 per cent and 21.6 per cent, respectively) as for those in the simple and paranoid groups (10.4 per cent and 11.6 per cent, respectively). This difference, he explains, is due to "heredo-constitutional elements" within the two groups. He tested his material with the method employed by Schulz and concluded that it is biologically homogeneous (which apparently signified homogeneity as to the main single gene). Böök (5), on the other hand, discusses the method used in both of these studies and concludes that it is impossible to disprove the existence of several independent recessive genes in schizophrenia. He feels, there are "endless possibilities to explain the fact that neither Schulz, nor Kallmann found any positive evidence in favor of genetic heterogeneity even though it is still there." Slater (41) has analyzed Kallmann's data on the frequencies of the Kraepelian types among children of probands in relation to types of psychosis in parents. He concludes, contrary to Kallmann, that the clinical forms are genetically heterogeneous.

As cited above, an array of independent genetic entities has been suggested as the biological basis of several classifications of schizophrenia. Leonhard (21), and adherent of Kleist's "splitting" concept, has divided schizophrenia according to the outcome into two groups: typical, with sharply distinguished subforms in later stages and characterized by a continuous deteriorative course; and atypical, characterized by a periodic, alternating and fluctuating course, generally with a more favorable prognosis. His "typical" cases showed much less apparent heredity than those in the other group. He suggests that the typical "defect-schizophrenias" can be viewed as degenerative conditions in Kleist's

definition, whereas the cerebral defect is less apparent in the atypical group.

Bleuler (4) also believes that he found a subgroup of schizophrenics without an hereditary taint and speculates that this subgroup may represent a separate disease within the large group of schizophrenias. Statistically, this distinction does not appear to be substantiated in his sample. Noteworthy is his conclusion as to the inherited substance of psychosis. He states that heredity is concerned with schizoid traits and reactive readiness either in the prepsychotic personality or in the course of the illness. He finds no evidence of a familial trend to actual dementia. Heredity has little or nothing to do with the progress of schizophrenia to dementia. (This opinion compares significantly with Slater's (42) observation that genotypic influence cannot be shown for deteriorative signs). Thus the schizophrenic disease process would consist of specific, schizoid, psychological mechanisms (with heredity assumed), and progressive dementia wherein the role of heredity is nil or little.

Biological unity of schizophrenia has also been tested through a study of the personality traits and complexes of psychotic symptoms within the families of patients. Wittermann (47) suggested that the heritable symptom complexes, from which psychosis may be composed, should be identified in an attempt to separate the inherited nuclei of psychosis from external influences. This approach, in his opinion, would facilitate the inquiry as to what is actually inherited in psychoses. He traced individual symptom complexes in members of several families and found definite similarities of symptoms among family members. Wildermuth (46) made a similar study and confirmed Wittermann's findings. Furthermore, he noted that patients with cyclic psychoses in whose families there were cases of schizophrenia developed atypical symptoms showing schizoid features. Schizophrenic patients from families manifesting cyclic psychoses themselves showed either a pronounced periodic course or affective features. Zehnder (48) has made a similar study concerning the similarity of clinical features in schizophrenia among siblings. She found equal proportions of sibships with similar or with dissimilar psychoses, respectively. She judged it surprising that differences in the type and course of the disease should occur at all, and concluded that heredity probably applies only to the schizophrenic syndrome as a whole, and that the individual clinical picture and course of illness are not determined by the genotype. Slater (41) reviewed Zehnder's data (comparing the sibs in pairs) and found that the distribution of Kraepelian types in pairs of sibs shows a strong positive correlation. Significant family resemblance was found as to the age of onset, the course and outcome of the disease, the extent of affective dilapidation, the presence of catatonic signs and the occurrence of states of excitement, depressive coloring and paranoid trends. No correlation was found as to destruction of the thought process. He concludes that family resemblance, although genetically determined, ought not to be interpreted in terms of the presence or absence of a specific schizophrenic gene. He found, for example, that the correlation coefficient for the age of onset was 0.55 ± 0.08, which corresponds closely to the correlation in weight among sibs (which in turn is accepted as evidence of polygenic determination). He concludes, therefore, that family resemblance in the characteristics of the psychosis is to be attributed to the action of common modifying genes. Penrose (32) arrived at a similar conclusion that multiple modifying factors determine the age of onset in schizophrenia.

The concept that familial, but non-specific genotypic factors may be operative in the common features of a psychosis has been variously emphasized by different workers. Apparently, non-specific familial resemblance links up with a more general inquiry: how much generality and how much specificity of response are there in an individual's behavior? It appears, moreover, that disorganization wrought by the psychotic process cannot be well separated from the individual operations of stimulus-response units within the affected personality. Hence, the working of polygenic or other familial modifiers can only be inferred rather than demonstrated outright.

Children of parents who were both psychotic are a logical group for this study. Thorough investigations of the children of two psychotic parents were done by Schulz (37) and by

Elsässer (7). Schulz found large numbers of schizophrenics among the children of parents with affective psychosis, whereas among the children of schizophrenic parents, manic-depressive psychoses are very rare. According to his observation both psychoses occur more frequently in the same families than would be expected on chance alone. This observation led him to speculate that there might be a genetic relationship between the two psychoses. To illustrate, he suggested a hypothetical system of alleles, AaBbCc, of which A causes the manifest psychosis to assume the manic-depressive form. Only those individuals who possess B and C could actually become psychotic, but only those who lack A and have a instead (in addition to B and C) could become schizophrenic. He found, furthermore, that schizophrenic children of schizophrenic parents show essentially the same clinical features as the schizophrenic children of normal parents.

Elsässer (7) found that the type of schizophrenia in children is not always the same as in the parents; he concludes that the Kraepelian forms are genetically interchangeable. The clinical picture depends less on the form and course of the psychosis in the family than on the age at which the individual breaks down. (A similar dependence upon the onset age has been observed by Slater (41).) Nevertheless, a certain basic type of psychosis can be traced within a family, showing modification according to age of onset. The psychoses of children born of two schizophrenic parents do not show a more severe course than is found in an average case. Only schizophrenic psychoses are found in children of schizophrenic parents. However, Elsässer himself states that one must select parents with typical schizophrenia. (For comparison he carefully discusses atypical psychoses.) He found, among other things, that in children of parents suffering from atypical psychoses the symptoms are similar to those in their parents. He suggests that the non-pathogenic genes within the family may have contributed to the resemblance of the psychoses. He even extends this notion to explain the differences between endogenous psychoses in general and holds that such differences may be determined by non-specific genotypes. One can detect in the trend of his reasoning a suggestion of the old one-endogenous-psychosis concept.

Summing up the specificity of the schizophrenic gene or genes has been suggested but not established by analyses of sibships and other familial groupings. Twin studies are more promising. No clear-cut case of monozygotic twins, where one twin is schizophrenic and the other manic-depressive, has ever been reported. However, most twin studies so far reported have lacked sufficiently full data to permit independent evaluation by subsequent workers. More extended data—both clinical and anthropological—should be provided in future twin studies. It is difficult to evaluate subjective observations where schizophrenia may give a definite coloring to other deviant behavior within family. Similarly, the presence of a gene for manic-depressive psychosis may appear to impart affective features or periodic course to schizophrenia found in the same sibship or family. However, it is conceded that even an experienced diagnostician can be influenced by his theoretical concepts of pathogenesis.

How is Schizophrenia Inherited? Results of Family Studies

In the analysis of pooled data concerning a fairly common disease, the geneticist looks first for indications of the most likely underlying mode of inheritance, for instance, whether dominant, recessive or intermediate. Secondly, he seeks the precise mode of transmission. The empirical expectancy rates expressing familial concentration of schizophrenia do not resemble any of the known Mendelian ratios. Complex hypotheses, some of them entirely arbitrary or even bizarre, have been devised in order to bridge the gap between empirical figures and tested modes of heredity.

The most widely postulated mode of transmission of schizophrenia is recessivity. In many instances it has been introduced mainly as a result of the impact of Rüdin's authority. Rüdin chose recessivity since the disease failed to appear regularly among the parents and the children of schizophrenic probands. Since Weinberg's sibship method did not reveal the 25 per cent requisite for a single factor recessive mode, but only a few per cent of the affected

sibs, he assumed two pairs of recessive genes to be responsible for psychosis.

Since subsequent investigations brought out higher values of expectancy rates for siblings than was the original Rüdin's figure, Luxenburger (24) came to the conclusion that a single recessive factor was a more likely interpretation of the empirical data than the double recessive mode of transmission, assuming a lowered penetrance of the genotype (60–70 per cent).

Kallmann (14), whose work is best known in this country because his monograph has been the only publication of its type in English language, came to similar conclusions. Furthermore, he suggested that somatic constitution was the modifying influence controlling not only the penetrance of the specific gene but also phenotypic variation (clinical forms) as well as the degree of malignancy. He elaborated upon Luxenburger's (23) concept of genetic linkage as the mechanism explaining the association between schizophrenia and tuberculosis, in that he postulated a parallelism between the severity of tuberculosis and the degree of concomitant regression of schizophrenia.

The operation of recessive inheritance is recognized, for instance, by an increased occurrence of consanguineous marriages or by higher percentage of affected persons among patients' sibs than among patients' children. The proof of a certain recessive mode, of course, necessitates testing by various approaches, taking into account gene frequency, mating patterns, etc.

Increased frequency of cousin marriages has not been reported in any large European series dealing with a population of average demographic characteristics. However, in some Scandinavian studies an increased percentage of consanguinity has been found. These were primarily studies of isolates. In a recent study of a remote district in northern Sweden, Böök (5) found that the incidence of cousin marriages among the parents of the schizophrenics was not increased; the incidence of schizophrenia in the local population was found to be about three times higher than in other populations. Kallmann (14) in a sample of average demographic characteristics found among parents of his probands about the same frequency of consanguineous marriages that prevailed in the general population. In his later studies (17) he found increased consanguinity in parents of the probands. It is difficult to interpret this increase, considering that schizophrenia is a fairly common disease.

A unique study of the incidence of schizophrenia in a population group characterized by a high degree of inbreeding has been presented by Weinberg and Lobstein (45). They investigated genetic aspects of mental disorder in the Jewish population of Amsterdam. Cousin marriages among the parents of schizophrenics were found to be higher than among the parents of patients suffering from manic-depressive psychosis. Unfortunately, the data on the frequency of cousin marriage in the Jewish population of Amsterdam were not available, and, thus, it cannot be determined if the 13.57 per cent of the schizophrenic probands descending from cousin marriages represents an increase. The authors suggested a higher incidence of schizophrenia among the sibs of the probands coming from cousin marriages than among those whose parents were not related. No case of schizophrenia was found in any of the 27 parental couples who were cousins. These findings certainly are suggestive of recessive heredity.

The ratio of the affected sibs to the affected children of schizophrenics has been the subject of a protracted controversy. This controversy is mainly of historical interest; the results have been inconclusive.

Recessivity has been tested also by means of reconstruction of various hypothetical constellations including frequency distribution of the mating patterns and magnitude of mate selection. These variables must be considered when the probability of a certain hereditary mode is tested as to its operation on population scale. Some of these investigations are interesting technically, but on the whole they are of historical value only. Generally this type of analysis has shown that it is difficult to fit the empirical data as a whole into a single factor type of recessive heredity.

Another line of evidence of recessivity has been followed in studying the children of two schizophrenic parents. Theoretically, all of

them should be schizophrenic if development of psychosis depended only on the main gene, identical in both parents; any reasonable figure less than 100 per cent could be explained by lowered penetrance. Luxenburger estimated the expectancy of schizophrenia in these children as 66 per cent, Kallmann 68 per cent, Schulz 38 per cent, Elsässer 39 per cent. These figures have been quoted in support of both the recessive and dominant modes. Since the hypothetical gene was considered the only determiner of psychosis, additional difficulties arose when expectancy rates had to be reconciled with concordance rates in identical twins. Various auxiliary explanations have been offered to explain the differences, all of them merely of speculative nature. Evidently, in identical twin partners all genes are identical, whereas the single born children of affected parents cannot be identical as to all of their genes and thus cannot show the same phenotype. Cases of children descending from two schizophrenic parents are certainly worthwhile studying from any viewpoint, but it would be imprudent to seek confirmation or disproof of the single factor theory in a few small samples. Such cases represent exceptional constellations, both biologically and in familial and personal relations.

In a simple dominant mode of transmission, the proportions of affected persons in parents, siblings and children should be approximately the same. If the manifestation is reduced, it should be reduced in all three generations equally. Reported expectancy rates do not fulfill this requirement. As is well-known the simple dominant transmission with complete manifestation is uncommon in human pathology. However, modifications of the dominant mechanism, especially when various degrees of manifestation in heterozygous state are considered, have been found useful in medical application. It is believed that the carriers of a common disease determined by a dominant gene would be eliminated by natural selection if the effect of the gene were not generally mitigated by modifying genes. Since modifying genes are assumed to be irregularly distributed in population, variations in severity are to be expected. This is certainly the case with schizophrenia so that the dominant mode would be a priori admissible. Investigations attempting to apply dominant theory have been forced to assume markedly reduced manifestation.

Various hypothetical possibilities of dominance have been discussed for instance by Schulz (38). He feels that dominance fits better with the empirical data than recessivity and with the assumption that the heterozygous state (Dd) is less penetrant than the homozygous state (DD). A double dominant mode explains the empirical data in a similar manner, in which case a penetrance of 0.50 can be postulated. The latter value would be closer to the concordance rates found in monozygotic twins. A heterozygote would have a formula Bb, Cc, and the presence of both B and C genes in the same complement of chromosomes would be necessary for the development of schizophrenia. Double dominance would not require a homozygous state for both the B and C genes for a full manifestation.

Direct analysis of individual pedigrees is the least promising method in psychoses. One can derive an impression of a definite mode of heredity by inspection of family trees, but generalized validity cannot be inferred from the behavior of the disease in individual families. Yet Patzig (29), apparently alarmed by the oversimplified assumptions of the "empirical-genetic-prognosis" school, resorted to the study of the transmission of schizophrenia in individual families and felt that psychosis can develop only through cooperation of a dominant main gene with secondary genes. He concluded that it is unlikely that schizoid psychopathy alone, even in a homozygous state (in double dose), could give rise to a process-psychosis. Penrose (32) states that some family histories may suggest a single autosomal recessive gene as a likely cause, others a single sex-linked recessive gene. No single gene can be held responsible for all cases.

Although most of the investigators worked on the assumption of one major gene difference, modifications of this mechanism have been suggested in terms of several major gene differences, cooperating in determination of schizophrenia. One or two of these hypothetical mechanisms have already been mentioned. Schulz (38) revealed his uncertainty as to the single factor determination by elaborating

upon various hypothetical modes of dominant transmission and stated that his suggested concept of dominance does not preclude the possibility of a triple dominant or even a determination by multiple genes. He advanced an interesting reasoning. If many genes are operative, it must be assumed, regarding the frequency of schizophrenia in the population, that most of the outwardly normal persons are heterozygous carriers of a certain number of schizophrenic genes. However, there will be at least one gene without which an individual cannot become psychotic. Such a gene would have a low frequency; otherwise, it would be difficult to explain the differences between the incidence of schizophrenia in the general population (0.8 per cent) and in children of schizophrenics (9–15 per cent). One could call only this one rare gene the specific gene for schizophrenia. Penrose (31) has pointed out that a high concordance rate in identical twins and a low rate in the fraternal twins or siblings could be best explained by a multifactorial mechanism. This suggestion might be applicable but has not yet been tested.

As mentioned in the introductory part of the article, major gene effect would best explain an organic etiology of schizophrenia, and is best compatible with the classical clinical concept of the disease. According to Muller (27) the mutant major gene (i.e., the form of gene causing the pathology) in most instances performs the same kind of action as the original "wild" gene, but its effect is less perfect. Thus a mutation of a "wild" gene usually results in a definite, specific deficiency or in a breakdown of a well-established chain of physiological reactions. Traits determined by a mutant major gene would not fit into a normal distribution curve because they represent separate categories. A category of deviant behavior must first be separable from all other variants of abnormal behavior as a specific entity if it is to be considered for testing as to compatibility with a major gene determination. Essentially, schizophrenia in the traditional concept can be separated from other forms of deviant behavior as a specific entity and, thus, meets the minimal requirement for a specific major gene determination.

It has been recognized relatively early that a single gene effect alone could not well account for psychosis, and various auxiliary mechanisms were suggested, reflecting new discoveries and attitudes in experimental genetics.

Modifying genes are most frequently suggested as cooperating with the specific gene. The concept of modifiers as an instrument of qualitative variation has been somewhat slow in gaining recognition in psychiatric genetics. It may be noted, for instance, that Luxenberger (26) thought in terms of genetically-determined inferiority of the connective tissue, in other words, an organ inferiority, which from a genetic viewpoint is a rather vague conception. In contrast, Lenz (20) interpreted the discrepancy between the expected and observed rates in sibs in terms of modifiers and environment. He felt that the low frequency of schizophrenia in parents of schizophrenics (assuming dominance) simply means that they are of normal health, possibly because they do not possess the modifiers that appear in their psychotic children. On the whole nothing definite is known about modifiers' effect in schizophrenia although it is widely postulated.

As far as could be found, determination of schizophrenia by polygenic systems has not been directly suggested. This is understandable not only because these clusters of genes having small, similar and quantitative effect have been studied only relatively recently, but mainly because they condition continuous variation. One thinks of them mainly in connection with normal traits. If one accepted the concept of schizophrenic reaction as a special constellation of essentially normal variables (similar to that which is assumed to cause psychoneurotic reactions), variable constellations of polygenic clusters would be a reasonable hypothesis. However, as mentioned before, the operation of polygenic systems in man has not yet been established.

We may summarize, then, by saying that the interpretation of the empirical rates of familial concentration in terms of a single gene has been, thus far, made possible by taking recourse to auxiliary hypotheses. The latter are of an arbitrary nature. The precise mode of heredity of schizophrenia remains unknown although there are some indications of recessivity. Several types of heredity determining frank psychosis are possible, and a multiple

factor causation is at least as likely as a single factor mechanism.

Results of Twin Studies

In the early period of scientific interest in twins, the cases were selected according to the oddity value, as for example, the instance of twins who developed delusions on the same day or in whom hallucinations were of an identical content. Such precision was expecting too much from heredity, and observers were inclined to overlook dissimilarities.

Luxenburger (22) was the first to introduce into the twin study the method of statistical sampling and thus to put the comparison of concordance on acceptable basis. Among his sample of 21 monozygotic pairs he found the psychosis in 66.6 per cent, which is the lowest value in the series of concordance rates in subsequent investigations. It has been duplicated in Rosanoff's (17) series of 41 monozygotic pairs (concordance 67.0 per cent), and it is reflected in the expectancy rate for children whose parents were both schizophrenic, as found by Luxenburger (66 per cent) and Kallmann (68 per cent). Luxenburger's fraternal twins showed concordance in 3.3 per cent. In no other material has such a low value been found. He had not reported his cases with clinical details because his primary interest was to show the difference in concordance between the monozygotic and dizygotic pairs.

The first systematic study of psychotic twins, analyzing in detail symptomatic development within the pairs and fulfilling at the same time the requirements of sampling and of modern determination of ovularity, was published by Essen-Möller (8). His sample consisted of 69 pairs of like-sexed twins, obtained from a total population of 10,000 patients admitted to several Swedish mental hospitals. Of these 69 pairs, 21 pairs were monozygotic. In only 7 of these 21 pairs were the probands schizophrenic; in 5 of them their partners were also psychotic or borderline cases. In none of the 5 pairs could the psychosis in the co-twin be diagnosed as typical schizophrenia although in 3 instances schizophrenic symptoms were noted. In all of these cases the dominant personality patterns would best be described as schizoid. Schizoid traits were found in yet another 4 pairs whose probands were not schizophrenic. Essen-Möller stresses the observation that, in spite of intra-pair differences in the diagnosis of the psychoses, there were also intra-pair similarities of the symptoms in the differently classified psychoses. He concluded that individual symptoms within the psychoses and the personality abnormalities which may have been present in the twins prior to the onset of the psychosis appear to be a more constant manifestation of an abnormal genotype than the psychoses themselves. As to environmental influences, he came to believe that significant intra-pair differences of environment are probably operative at an earlier stage of the individual's development than is generally assumed. He feels that personality differences can be traced to an earlier period of life than the tested environmental influences. Essen-Möller's report is notable in that no instance of concordance as to typical schizophrenia had been found.

The largest collection of schizophrenic twins has been gathered together by Kallmann (17). By 1952, he had calculated concordance rates on as many as 685 dizygotic and 268 monozygotic pairs. He gives rates of concordance as 86.2 per cent for monozygotic and 14.5 per cent for dizygotic pairs. The above rate for monozygotic pairs is probably the highest on record, signifying that a co-twin of a schizophrenic proband case is likely to become schizophrenic also in 86.2 per cent of all instances. Kallmann's twin studies are widely known in the psychiatric field, and, therefore, his observations need not be reported in detail. Most remarkable is the circumstance that he has found no monozygotic pair in which one twin is schizophrenic and the other carries a diagnosis of other psychosis. Furthermore, he found that the physically more resistant of the twins, as revealed by his greater weight, was usually either free of psychosis or his illness was milder. He illustrated this concept by three twin case histories (16). Methodologically, Kallmann recommends a combination of twin study with a sibship study under the term "twin-family method". The aim of this procedure is to obtain expectancy rates in a continuous series of relatives, graded according to the closeness of consanguinity to the proband. The series consists of expectancy rates in step-siblings, half-siblings, full-siblings,

fraternal co-twins, and identical co-twins. Thus, the rates are expected to be lowest for step-siblings and highest for identical co-twins. It has been demonstrated by Kallmann's studies (15) that this orderly sequence of graded values can be arrived at even when the material is heterogeneous, as when the ordinary sibships and the twins are obtained from different samples. In a discussion of investigative methods Allen (1) points out that the combination of older style twin study with the usual family method, although having the advantage of obtaining both types of data for one set of probands, adds nothing new. He recommends a study of monozygotic twins, separated into concordant and discordant groups. In this manner a group with predominantly genetic effect and another group with predominantly environmental effect will be available. This interesting approach has not yet been tested on psychological traits, where admittedly the dividing line between the genotypic determination and environmental effect is not as clear as in most somatic traits.

Slater has recently (42) published a study of psychotic and neurotic illness in twins and their families together with detailed clinical information. He retained full homogeneity in his sample by confining it to the families of his twins alone. His report is distinguished by a consistent application of an original dermatoglyphic method in determination of ovularity (zygosity) and by conservative conclusions. He finds the concordance rate in monozygotic pairs to be 76 per cent and in dizygotic pairs 14 per cent. He estimates the incidence of schizophrenia among the sibs at 5 per cent. Taking all classes of relatives together, there is strong evidence that the type of onset of schizophrenia, when classified as sudden, gradual with sudden exacerbation, and gradual, is genetically determined. No correlation is found between the health and physique of the twins and their developing a psychosis. There is no observable predisposition to psychiatric illness on the part of the twin who was smaller at birth. Emotional instability, hysterical tendencies and paranoid trends show universal association with more serious illness, but actual psychogenic precipitation appears of scant significance. There may be a physical precipitation in the identical twin and psychogenic causation in the co-twin, as for instance, childbirth psychosis in one and guilt feelings over not having children in the other.

According to Slater identical twins differ very little in the degree of neuroticism in childhood, and when there is a difference, there is no relationship to mental health in adult life. In all diagnostic categories involving fraternal twins, the twin who was more neurotic in childhood tended to be more severely afflicted in adult life. In both identical and fraternal twins the more severe illness tends to be in the more submissive partner. This finding suggests the influence of environmental psychological causes.

In a detailed analysis of catatonic signs and symptoms in the individual, Slater found that identical twins resemble one another significantly as to occurrence of these features. All classes of relatives showed a significant tendency to resemble one another in mood changes, the most striking resemblance being the occurrence of depression. On the other hand, deteriorative symptoms showed little evidence of being genetically determined. (M. Bleuler (4) arrived at similar conclusions.)

These observations by Slater show that fresh approaches are being added to traditional procedures in twin studies.

Summing up twin studies, it is seen that the main objective, comparative investigation of concordance, has been achieved. It has been demonstrated on hospital patients that there is a significant increase in concordance in monozygotic pairs. Since it is a reasonable assumption that practically all cases of classical schizophrenia become, at least temporarily, members of hospital populations, the conclusions can be considered of general validity. The absolute values of concordance rates, advanced by different investigators, are of less importance than the ratio of concordances between the two ovularity categories. The significant and probably preponderant role of the genotype in the determination of schizophrenia appears, therefore, to be well established by these investigations. However, little use has been made, thus far, of the twin method study for comparative developmental investigations covering the full life span of the individuals.

It should be emphasized that in all studies

in the neuropsychiatric field the usual technical difficulties inherent in the genetic investigation of human traits are much increased. A major problem is the reliability of diagnosis. Usually at least two generations are studied, and this circumstance involves differences in diagnostic approach and terminology. Statistical corrections, inevitable in problems dealing with other than congenital traits, can slant the results. Furthermore, attention has been given to the demographic aspects of the material often out of proportion to the attention paid to the central problem, which ought to be concerned primarily with pathogenesis.

The Place of Schizoid Personality in the Genetic Interpretation of Schizophrenia

An increased incidence of cases of schizoid personality within the families with schizophrenic patients has been reported by most investigators. More precisely, the pertaining expectancy rates have been taken as increased on observer's impression only because no regular ascertainment in a normal population sample has been available for comparison.

Several authors believe that the specific gene in the heterozygous state (in a single dose), irrespective of whether it is dominant or recessive, may show itself clinically as schizoid personality. This might be a sound concept genetically if supported by a reasonable minimum of evidence. The concept of a partial or modified main gene effect in single dose had been developed apparently in order to bring the genetic theory in further agreement with certain pathogenetic interpretations of schizophrenia. The single specific determiner of the Kraepelian disease entity had to be integrated into the diffuse Kretschmerian units of body type and personality. Genetically this could not work because Kretschmerian body types and personalities are not traits which could be interpreted in single gene terms. In fact, Kretschmerian types and personalities are conceptual constructs rather than typical Mendelian traits. Obviously, the ascertainment and clinical classification of personality disorders among the relatives of hospital patients are bound to be less reliable than the case finding of full psychoses, especially in large scale studies. Inasmuch as in psychiatry the gathering of genetic evidence often parallels the type of clinical persuasion of the individual investigators, one wonders if the excess of schizoid personalities would have been found had schizophrenia been regarded as pathogenetically independent of any personality pattern. The criteria and means of diagnostic evaluation are rarely given with such detail that other workers could check them against their own clinical views. A notable exception is Slater's (42) report, giving a candid description of a practicable procedure. The classification of behavioral oddities was made on the descriptions of friends and relatives, and the deviant pattern thus constructed has been identified as a "vague picture of schizoid personality". Final evaluation of the observations is given in cautious, non-statistical manner. It is stated that the abnormal personalities in the schizophrenic families were more markedly abnormal than those found in the affective families. Paranoid personality trends were most frequent in the parents, sibs and children of schizophrenics. Psychopaths were very often found in the families of schizophrenics. Elsässer (7) is probable the only investigator who has not found an accumulation of schizoid personalities among children of probands although both parents of his studied sibships were schizophrenic. He considers this finding significant.

Most investigators have long felt that schizoid personality represents essentially a modified manifestation of the main schizophrenic genotype in the unitary causation concept. In this connection it is interesting to note that as early as 1926 Hoffmann (13) stated that schizoid personality is a diagnostic category comprising a number of entities. One should not investigate the mode of inheritance of schizoid personality as a whole, but instead one should analyze genetically the separate qualities (traits) constituting the personality. Schulz (38) thinks that there is only one type of schizoid personality, whereas Hoffmann's concept implies diversity. Furthermore, believing there is only one type of schizophrenia, Schulz objects to postulating a number of different genotypes for schizoid personality in addition to the main schizophrenic gene.

Luxenburger (26) has pushed the unitary genetic concept to an extreme by recognizing

as a true schizoid personality only those cases which occur in a family with a schizophrenic patient. In an endeavor to connect the genetic approach with Kretschmer's constitutional concepts, he built an arbitrary circle of heredity ("Erbkreis") of schizophrenia. Starting from the observation that the schizophrenic family features are distinguished by a definite, though vaguely described coloring through the prevailing body build and temperament, he grants specific genetic significance to any physical or mental aberration which can be somehow linked with schizophrenia. Thus, tuberculosis has its place in the "Erbkreis" because of the alleged close genetic correlation between the susceptibility to tuberculosis and schizophrenia. The common denominator is supposed to be the inability to form adequate connective tissue, and, thus, there is overlapping into the "Erbkreis" of the connective tissue weakness. The latter results from defective mesodermal development, manifested by paucity of pigment and leptosomia. Furthermore, there is overlapping with status dysraphicus. Apparently, an ideal representant of the "Erbkreis" would be a blond, blue-eyed, tubercular schizophrenic with a concealed spina bifida, and supported by flat feet.

A graded series of personality patterns, stemming from the schizophrenic gene, has been proposed by Luxenburger to complement the physical "Erbkreis". He believes that the schizophrenic "anlage" can turn a normal personality into a schizothymic one. A schizoid psychopath would arise from an ordinary psychopath, and, in general, schizopathic coloring could be afforded to any psychosis. In the organic psychoses, the influence of schizophrenic gene could be understood as a "pathoplastic" effect, while in the endogenous psychoses it would be interpreted as a "mixed condition". According to this concept all psychoses, psychopathies and neuroses, with schizoid coloring belong in the heredity circle of schizophrenia, no matter what the underlying disorder might be. This concept might lead to a sound nosologic system if it could be substantiated by genetic evidence. Luxenburger may have derived this concept of an ubiquitous schizoid encroachment, not so much from clinical reasoning as from the consideration of the high frequency of the schizophrenic genes in the population. He apparently felt that some manifestation would be inevitable.

The genetic status of schizoid personality can hardly be described exclusively in terms of a major gene effect. Since the transition from normal to deviant personality patterns is imperceptible, and normal personality traits can be evaluated quantitatively in terms of personality dimensions, a multifactorial determination should be considered. A partial major gene effect certainly can be visualized as showing itself clinically in schizoid disorganization of personality, but it cannot explain everything.

Inasmuch as we classify any degree of schizoid behavior only on symptoms, it is clear that a sharp line cannot be drawn between an attenuated genetic psychosis and a schizoid disorganized personality. On clinical experience it would seem that there is a genetic overlapping between degrees of disorganized personality of schizoid type, including schizophrenic psychosis. However, it is equally difficult to draw a line between schizoid and normal personalities. It is, therefore, difficult to attribute all schizoid personalities to the same factor as schizophrenic psychosis. This may not be necessary even under a unitary hypothesis of schizophrenia. It has been shown for mental deficiency (Fraser-Roberts (10)) that syndromes displaying continuity when evaluated by symptoms can be determined by several independent mechanisms. This shows, furthermore, that conditions which are of separate origin (organic or psychological) can form a symptomatic (phenotypic) continuum.

If we accept this view of schizophrenia and schizoid personality, the selection of index cases from hospitalized schizophrenics is to be regarded as a method imposed by expediency. In fact, cases of schizoid personality discovered independently of any family association with schizophrenic psychosis should be considered legitimate probands in their own right. They should be equivalent to the cases of full psychosis as to the specific genes. Investigators postulating the attenuated major gene conditioning of schizoid personality seemingly have not been aware of this technical inference of their views.

Unless an objective, biological diagnostic

test is available, any inference on the genetic basis of schizoid personality is entirely arbitrary. We are unable to decide if there is a biological continuity corresponding to the symptomatic continuity from normal to psychotic behavior. Yet on clinical grounds, the existence of a core of true schizophrenia, perhaps together with a group of related personality types, is undeniable. The genetic position of the related personalities remains unclear.

Discussion and Summary

The expansion of psychological studies with all its promise as well as lack of major discoveries in the organic aspects of psychoses has led to a neglect of biological inquiry in psychiatry. Thus, it is necessary to justify the propriety of a genetic concept as a primary etiologic factor.

As is well-known, not all persons under similar stress develop mental disorder. Furthermore, individuality is based primarily on chromosomal uniqueness. Thus, individual differences in capacity of adaptive response by different behavior lead to the concept of genic determination.

Environmental influences and heredity cannot well be disentangled quantitatively when one studies their relative contributions to the genesis of deviant behavior. It is understood that their respective effects cannot be simply additive. Thus, it is of practical importance to realize that the relationship between genotype and environment constantly changes from one situation to the next, and throughout life. For purpose of psychiatric study, we need to be aware that some genes make themselves outwardly perceptible through the clinical phenotype under almost any constellation of the genic milieu, somatic constitution and external stimuli, whereas the presence of other genes is less readily discernible or may be completely concealed.

Essentially, there is no real controversy in the nature-nurture problem. Some put heredity first, whereas others stress environment, depending on personal predilection.

Schizophrenia is not transmitted regularly from one generation to another, nor does it show the typical Mendelian distribution in sibships. Thus, evidence of heredity is to be sought in familial concentration and in comparison of concordance between identical and fraternal twins, where neither of these phenomena can be explained environmentally. The data herein reviewed prove a clearly familial concentration. The ratios of familial to population incidence, as they have been reported in investigations of varied populations, are compatible with ratios occurring in a fairly common heritable trait. An environmental explanation of the difference between the familial and population distribution of schizophrenia has not been found. Furthermore, the studies of twin-samples quoted in this review have established that schizophrenia develops in both members of a pair more frequently in identical than in fraternal twins. Environmental differences alone would not account for the differences in concordance rates.

No further conclusions can be safely derived from the available genetic data other than the significant role of the genotype. Genetic studies have failed, so far, to establish the genotypic unity of schizophrenia.

Usually, a single gene of major effect is postulated as the determining factor of all forms of schizophrenia. With equal claim to validity, the data could be interpreted as the effect of multiple genes. Moreover, schizophrenia might well comprise several genetic entities with different genetic mechanisms. Finally, it can be assumed that a certain proportion of the diagnosed schizophrenic reactions are probably not dependent on a specific genotype. It is uncertain whether a recessive or dominant type of heredity is involved although there are indications of recessivity in some instances. A precise analysis of the data with the view to specifying the mode of heredity is of little avail so long as the question of the biological unity of schizophrenia remains in dispute.

A precise identification of the genic mechanism, in itself, would furnish no information as to the relative contribution of the environmental effect. Thus, the hypothesis of a major gene as the cause of psychosis does not necessarily imply that the gene asserts itself under any environment. The limits of environmental influence could be seen more clearly if all carriers of the specific gene were identified.

It has been suggested that disorganized personality with schizoid features, not attain-

ing the clinical level of a frank psychosis, is an expression of a true schizophrenic genotype modified by the individual's non-specific genic background. The pertinent genetic analyses have failed to substantiate this assertion. Of course, one might speculate that specific gene or genes are responsible for the substance of the psychosis, while other genes provide the background for personality coloring.

The results of psychiatric genetic research and its present status can be best judged in the historical perspective. Modern psychiatric genetics was stimulated by the establishment of the first workable psychiatric nosology and by the early surge of Mendelism. Thus, the idea of one gene difference corresponding to each Kraepelian entity fitted well into the genetic and psychiatric concepts of that period. Bleuler's revision brought some uneasiness into the straight concepts of Rüdin's school and led certain investigators to doubt the validity of the unitary genetic interpretation. Surprisingly, the diffuse Kretschmerian concepts have not been rejected by Rüdin's school although nothing could be more foreign to the rigid delimitation of the single gene difference than the overlapping somatic and personality types. Today we are thus reminded that Kretschmerian types were seen as clearly circumscribed, static entities, and that continuous variation and dynamic development were unfamiliar concepts. On the whole, the German genetic school did not follow the development of modern psychiatry beyond Bleuler and Kretschmer. Inasmuch as psychiatric genetics has been largely dependent on the original German school, recent additions merely emphasize the original findings.

Evidently, the basic question as to what is actually inherited cannot be answered. Undoubtedly, a specific metabolic error would fit best into a genetic scheme, but there is no convenient enzyme in sight. Inheritance of vulnerability is often mentioned, but such formulations only spotlight our ignorance. Needless to say, a gene-determined metabolic error would not entirely explain the pathogenesis.

In summary, the genetic study of schizophrenia has provided much important information regarding the natural history of the psychoses. It has given a biological meaning to the evaluation of the family history: the genesis of deviant behavior may now be studied in terms of family units.

Finally, in the light of evidence herein reviewed, genetic factors do have a co-determinative and most likely a specific significance in the development of the typical schizophrenic psychosis.

BIBLIOGRAPHY

1. Allen, G.: Discussion in: Conference on problems and methods in human genetics. *Am. J. Human Genet., 6:* 162, 1954.
2. Anastasi, A.: The inherited and acquired components of behavior. In *Genetics and the Inheritance of Integrated Neurological and Psychiatric Patterns.* Res. Publ. Ass. Nerv. Ment. Dis., Vol. 33. Baltimore: The Williams & Wilkins Co., 1954.
3. Batchelor, I. R. C.: Repeated suicidal attempts. *Brit. J. M. Psychol., 27:* 158, 1954.
4. Bleuler, M.: Vererbungsprobleme bei Schizophrenen. *Z. Neur., 127:* 321, 1930.
5. Böök, J. A.: A genetic and neuropsychiatric investigation of a North-Swedish population. *Acta Genet., 4:* 345, 1953.
6. Brown, F. W.: Heredity in the psychoneuroses. *Proc. Roy. Soc. Med., 35:* 785, 1942.
7. Elsässer, G.: *Die Nachkommen Geisteskranker Elternpaare.* Stuttgart: Thieme, 1952.
8. Essen-Möller, E.: *Psychiatrische Untersuchungen an einer Serie von Zwillingen.* Copenhagen: Munksgaard, 1941.
9. Eysenck, H. J.: *Dimensions of Personality.* London: Kegan Paul, 1947.
10. Fraser-Roberts, J. A.: The genetics of oligophrenia. In *Congrès International de Psychiatrie (1950),* Vol. 6. Paris: Hermann, 1952.
11. Fremming, K. H.: *Morbid Risk of Mental Diseases and Other Mental Abnormalities in An Average Danish Population.* Copenhagen: Munksgaard, 1947.
12. Haskell, G.: Contributions of heredity and environment to manifestations of psychoneurosis. *Am. J. Human Genet., 5:* 236, 1953.
13. Hoffmann, H.: *Familienpsychosen in schizophrenem Erbkreis.* Berlin: Karger, 1926.
14. Kallmann, F. J.: *The Genetics of Schizophrenia.* New York: Augustin, 1938.
15. Kallmann, F. J., and Barrera, S. E.: The heredoconstitutional mechanism of predisposition and resistance to schizophrenia. *Am. J. Psychiat., 98:* 544, 1942.
16. Kallmann, F. J.: Heredity and constitution in relation to the treatment of mental disorders. In *Failures in Psychiatric Treatment,* P. H. Hoch, Ed. New York: Grune & Stratton, 1948.
17. Kallman, F. J.: *Heredity in Health and Mental Disorder.* New York: Norton, 1953.
18. Kattentidt, B.: Zur Frage einer Belastungsstatistik der Durchschnittsbevölkerung. *Z. Neur., 103:* 288, 1926.
19. Larsson, T., and Sjögren, T.: A methodological, psychiatric and statistical study of a large swedish rural population. *Acta Psychiat. et Neurol., Suppl. 89:* 1954.
20. Lenz, F.: Mendeln die Geisteskrankheiten? *Z. ind. Abstam. u. Vererb.-Lehre, 73:* 559, 1937.

21. Leonhard, K.: *Die Defekt-schizophrenen Krankheitsbilder*. Leipzig: Thieme, 1936.
22. Luxenburger, H.: Vorläufiger Bericht über psychiatrische Serienuntersuchungen an Zwillingen. *Z. Neur., 116:* 297, 1928.
23. Luxenburger, H.: Über weitere Untersuchungen zur Frage der Korrelation von schizophrener Anlage und Widerstandsschwäche gegen die tuberkulöse Infektion. *Z. Neur., 122:* 74, 1929.
24. Luxenburger, H.: Untersuchungen an schizophrenen Zwillingen und ihren Geschwistern zur Prüfung der Realität von Manifestationsschwankungen. *Z. Neur., 154:* 351, 1935.
25. Luxenburger, H.: Bemerkungen zu dem Vortrag von F. Lenz. *Z. ind. Abstam. u. Vererb.-Lehre, 73:* 565, 1937.
26. Luxenburger, H.: Die Schizophrenie und ihr Erbkreis. In *Handb. d. Erbbiologie*. G. Just, Ed., Vol. 5, Berlin: Springer, 1939.
27. Muller, H. J.: Further studies on the nature and causes of gene mutations. *Proc. 6th Int. Cong. Genet., 1:* 213, 1932.
28. Neel, J. V.: On some pitfalls in developing an adequate genetic hypothesis. *Am. J. Human Genet., 7:* 1, 1955.
29. Patzig, B.: Untersuchungen zur Frage des Erbganges und der Manifestierung schizophrener Erkrankungen. *Z. Neur,. 161:* 521, 1938.
30. Penrose, L. S.: Survey of cases of familial mental illness. *Digest Neurol. & Psychiat., 13:* 644, 1945.
31. Penrose, L. S.: The genetical background of common diseases. *Acta Genet., 4:* 257, 1953.
32. Penrose, L. S.: *The Biology of Mental Defect*. London: Sidgwick & Jackson, 1954.
33. Planansky, K., and Allen, G.: Heredity in relation to variable resistance to pulmonary tuberculosis. *Am. J. Human Genet., 5:* 322, 1953.
34. Rüdin, E.: *Zur Vererbung und Neuentstehung der Dementia Praecox*. Berlin: Springer, 1916.
35. Rüdin, E.: Über Vererbung geistiger Störungen. *Z. Neur., 81:* 459, 1923.
36. Schulz, B.: Versuch einer genealogisch statistischen Überprüfung eines Schizophrenie-Material auf biologische Einheit. *Z. Neur., 151:* 145, 1934.
37. Schulz, B.: Empirische Untersuchungen über die Bedeutung beidseitiger Belastung mit endogenen Psychosen. *Z. Neur., 165:* 97, 1939.
38. Schulz, B.: Kinder manisch-depressiver und anderer affektivpsychotischer Elternpaare. *Z. Neur., 169:* 311, 1940.
39. Slater, E.: The inheritance of manic-depressive insanity. *Proc. Roy. Soc. Med., 29:* 981, 1936.
40. Slater, E.: The neurotic constitution. *J. Neurol., Neurosurg. & Psyhiat., 6:* 1, 1943.
41. Slater, E.: Genetical causes of schizophrenic symptoms. *Monatsschr. Psychiat. u. Neurol., 113:* 50, 1947.
42. Slater, E.: Psychotic and neurotic illnesses in twins. Medical Research Council, Special Report No. 278. London: H. M. Stationery Office, 1953.
43. Strömgren, E.: *Beitrage zur Psychiatrischen Erbkunde*. Copenhagen: Munksgaard, 1938.
44. Strömgren, E.: Social surveys, *J. Ment. Sc., 94:* 266, 1948.
45. Weinberg, L., and Lobstein, J.: Inheritance in schizophrenia. *Acta Psychiat. et Neurol., 18:* 93, 1943.
46. Wildermuth, H.: Geschwisterpsychosen. *Z. Neur., 110:* 60, 1927.
47. Wittermann, E.: Klinische Psychiatrie und Familienforschung. *Z. Neur., 105:* 459, 1926.
48. Zehnder, M.: Über Krankheitsbild und-verlauf bei schizophrenen Geschwistern. *Monatsschr. Psychiat. u. Neurol., 103:* 231, 1941.

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FACIAL PHANTOM PHENOMENON[1]

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In a previous paper on a review of the literature of phantom phenomena (21) it became quite clear to this author how little was mentioned about phantom facial parts. Not one of the many excellent articles and books having to do with facial disfigurement even mentioned its existence. Barsky (4), in his book on plastic surgery, makes frequent comment about the psychological aspects. He pleads for the plastic surgeon to "make every effort to comprehend the patient's mental attitude." Berndorfer (5) in discussion of "Plastic Surgery, Physiognomy, and Psychoanalysis" refers not at all to this phenomenon. The same could be said for the detailed publications by Young (32), Updegraff and Menninger (31), Abel (1, 2) and that thorough monograph by MacGregor *et al.* (25). No remark of even the possibility is to be found in the studies of Hill and Silver (20), Baker and Smith (3), or Rosen (27). Deutsch and Murphy (7) in their discussion of phantom parts as "Remembrance of Things Past" make no indication of the facial phantom nor does Schilder in his "Medical Psychology" (29) or "The Image and Appearance of the Human Body" (30). As a matter of fact, after very close scrutiny of the available literature the only reference in which this syndrome could be found was the very illuminating and provocative article by Gallinek (19). He claimed never to have observed a phantom after facial disfigurement or after amputation of the mamma or penis. This seemed particularly confounding especially since one would expect, as Gallinek further suggested, that according to psychoanalytic principles, if anything, phantom facial parts would be anticipated more rather than less often after amputation.

Prompted by curiosity about this apparent incongruity and inconsistency, this author investigated several instances of facial part amputation as the initial step in further, more detailed studies of phantom phenomena. The following case reports and subsequent discussion are to be considered the preliminary effort in that direction.

Mr. J. L. G. (figure 1), a 69-year-old, white, married, right-handed mason, resident of Columbus, Ohio, was admitted to the University Hospital on 7/26/54 for treatment of left facial pain of nine weeks' duration. Approximately three weeks prior to this admission, he was seen at the University Clinic for a general check-up. At that time, it was suspected that what was previously diagnosed as "sinus trouble" was more serious. He was told it was cancer and advised to have surgery performed immediately. He agreed only if "you'll take it all out if I go on the operating table and take out the eye too 'cause it's hurting me." Two days after admission, a Caldwell-Luc operation was performed, and because the biopsy of the antral sinus revealed a moderately well differentiated squamous cell carcinoma, a left radical maxillectomy was performed along with a partial left hard palate removal and left enucleation. (The patient believes his eye was fixed in alcohol and studied and expressed this with no particular concern.) His post-operative course was relatively uneventful, and just before discharge on 9/3/54, he received several x-ray treatments locally and a rubber sponge prosthesis to fill the marked depression in the left maxillary region and hard palate defect. He has been followed periodically in the Ear, Nose, and Throat Clinic since leaving the hospital.

At present, the patient complains of visual difficulty such that at a distance of approximately 45 to 75 feet objects appear double. Frequently, the patient has the sensation that the eyebrow hairs are scratching his orbit, and he still attempts to see if he has grown an eyebrow on the left (which he hasn't) by using a mirror. Mr. G. prided himself on being an extremely accurate judge of distance prior to surgery. However, following the enucleation, he has lost this capacity. . . ."Now I don't do as good. I'm afraid to measure length without a ruler . . . every once in awhile at night when

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FIG. 1

there's a small light in the room, never at night without a light, and my right eye is tired, I take my glasses off and I see a thin thread-like up and down beam of light about five inches long. It stays in one place. Maybe it could be the end of a nerve going to the eye. . . . I couldn't believe it myself so I covered my good eye with my hand and a wet cloth. I told my wife but she laughed at me and said I was going crazy. I was afraid the doctors would say the same thing so I just didn't tell them." Additional complaints include poor speech and inability to drink, especially without the hard palate prosthesis. Even with the prosthesis, sucking from a straw or drinking from a fountain is not possible.

As for his social and occupational relations, the patient is active in church affairs, visits frequently, and does not work "except around the house." Although the patient is embarrassed when he notices people staring at him and "the hole in my cheek", there is very little further concern expressed except its denial with fatalistic submission. . . . "I wasn't worried a bit when I knew it was cancer. I suffered in this world and if it was time to go, I was ready."

The past medical history reveals no unusual diseases or complications of the usual ones. The patient revealed that he had several temper outbursts "it took a lot to stir me up and then I was mean and the devil himself couldn't cope with me. I even took a hammer and hit a man with it." In the family, the patient was the fourth youngest of fourteen siblings of his mother who died at "96 years, 3 months, 27 days." "She never wore glasses in her life and did fine needlework until she died."

Mr. C. W. (figure 2), a 57-year-old patient of the Columbus State School, was admitted to the University Hospital on 1/4/53 for treatment of left maxillary sinus squamous cell carcinoma of approximately two months' duration.

In November of 1952, this patient whose I.Q. was recorded as 40 was noted to have had a proptosis of the left eye. One month later, a biopsy was taken of "an irregular area in the left upper palate". Three days after admission to the University Hospital, a radical resection of the left maxillary sinus and left enucleation, and resection of the coronoid and condyloid process of the left mandible were performed. At operation, marked invasion of the cranial base was noted. Post-operatively, he received x-ray therapy to the area until and after discharge on 1/20/53 and until 5/14/53. On return to the State School, he continued on the hospital unit without returning to his regularly assigned manual labor. On 8/9/54, the patient died after several neoplastic hemiplegias and hemianesthesias and a terminal hyperpyrexia and shock.

Little is known about Mr. W.'s familial history except that the mother, a sister, and a brother were also mentally retarded. The patient himself was admitted to Columbus State School on 9/14/19 at about 11 years of age and had been there since as a patient and handyman.

Five months prior to his death, the patient was seen in psychiatric interview. Complete and detailed communication was difficult because of his limited intellectual capacity and a marked speech deficit. He indicated by drawings and response to direct questioning that he

FIG. 2

felt at times that both his eyes were present though he was quite well aware that in actuality his left one was missing.

Mr. R. L. W. (figure 3), a 50-year-old, white, twice-married, former dry cleaning store owner, of Reynoldsburg, Ohio, was admitted to the University Hospital on August 3, 1954, for treatment of progressing neoplastic lesion of the right side of the face and nose of approximately seven years' duration. While shaving about seven or eight years ago, the patient noticed a "white-head" at the inner canthus of the right eye. This persisted and spread in spite of all the home remedies and even after treatment by the local medical doctor and "grandmother's salves". Finally, in July of 1954, he was seen in the University Cancer Clinic where a diagnosis of basal cell and squamous cell carcinoma of the face was made. On August 10, 1954, surgery was performed with removal of the zygoma and maxillary bone without entering the antrum. Almost the entire nose was absent, and a split thickness graft was applied with some moderate success. Towards the end of his hospitalization and after his discharge on August 25, 1954, he received x-ray therapy to the face.

On the average of once a week, Mr. W. gets an itching sensation at the tip of the nose which is no longer present, and there is a marked compulsion to scratch it or relieve the itching by wiggling the face or mouth. Mr. W. frankly admitted not revealing this previously because he was fully aware that "it was abnormal to have an itching in a nose that wasn't there so I

FIG. 3

FIG. 4

just didn't tell anyone." He stated that preoperatively he had never had any serious illnesses, but since the operation, he has become "nervous, shaky, and frightened". Immediately after the operation, when he first saw his head "bandaged like a mummy", he thought, "my goodness, will he ever be able to put a nose back on again; will I look normal again; can I face people again." He has withdrawn from all social contacts except when absolutely necessary and tries to arrange these for the night time. He has sold his dry cleaning store and now supports himself marginally with odd jobs.

The past medical and familial history is essentially non-contributory.

Mr. R. B. (figure 4), a 68-year-old, white, married, ambidextrous, unemployed, former house painter of North Baltimore, Ohio, was admitted to the University Hospital for treatment of a left maxillary sinus carcinoma of approximately two months' duration. In early August, 1954, the patient went to his local medical doctor because of a persistent "head cold". After symptomatic treatment proved of no benefit and a left proptosis and left cheek swelling became increasingly evident, he was referred to the University Ophthalmology Clinic where a diagnosis of carcinoma of the maxillary sinus was made. . . . "I was a goner." He was admitted to University Hospital on 8/30/54, and 10 days later a left radical maxillectomy and enucleation were performed. His post-operative course was uneventful except for periods of depression which responded to such self-advice as "get out of it and if this is the end, that's it." About the lost eye: "I don't know what they did with it. It didn't make a bit of difference. It's gone." On 10/3/54, he was discharged from the University Hospital.

Not infrequently, Mr. B. feels the lost eye is still present, especially when its use would ordinarily be required. For example, "if I want to sight something, I'll kinda' blink that (missing) eye even though I know I don't have either the upper or lower lid. I feel like my eye is still there then and so to check it, I look in a mirror and at times I imagine I see the eye and the lids and even with the pupil in it. . . . . At other times it feels as though there's something in it and I want to rub it." Especially immediately after the operation, the patient had difficulty estimating fore-and-background and "at first I'd grab for something which wasn't there . . . now I have to concentrate." Although gradually Mr. B. is getting back with his former crowd after an initial withdrawal, he is occasionally hurt and embarrassed when special reference is made of his eye, as for example when the children in the street call him "Mr. Patch Eye".

The personal and familial histories reveal no marked physiological or psychological abnormality.

DISCUSSION

As with any symptom the significance of the phantom phenomenon should be considered in terms of its genesis, its meaning, and its economy. In the formation of self-concept of self-image there are two processes which can be considered 1) reactions to other's reactions to self or others-self and 2) one's own reaction to self or self-self reactions. In each case the response is mediated by centripetally directed

sensory afferent impulses. As a test of the validity of these concepts, centrifugally directed motor efferent behaviors are set up, and the responses evoked determine not only the previous evaluation of one's self to the self, but also set up a new series of chain reactions, each for further initiation and consequent integration and elaboration. This takes place along complex and dynamically operating physiological and psychological channels which are in actuality but two aspects of a unity. Further, it would seem most important to concentrate our efforts in the region of the ego boundary which Federn considered very much a type of sensory organ.

In regard to genesis of phantom phenomenon, one of the barriers which might be considered as interfering with maximally efficient operating ego dynamics is the loss of a part of the body. The acceptance of this loss will depend on many factors, not the least significant of which are the anatomical location of the part, its physiological and psychological significance, the nature of the loss, including the acuteness and chronicity, and the time and state of development of the total personality at the moment of loss. It has been shown (20), for example, that if there was a congenital absence or loss before birth, so to speak, a phantom will probably not result. This may be due in part to a lack of development or poorly developed body ego. If the loss is early in development and especially where there has been relatively little organ libidinous investment, the likelihood of a phantom after amputation of that organ would be decreased. Thus, when amputation occurs before the age of six, there would be only slight expectancy of a phantom. If the loss were acute in the later stages of psychological development, there would be relatively little chance to reestablish equilibrium because minimal opportunity exists for reinvestment or cathexis of the libido. The opposite, then, would be observed in chronic losses.

The meaning of the phantom can be understood as the attempt by the ego or the self at reorganization so as to maintain the body image and scheme gestalt. There is a remarkable degree of inability to accept less than totality in this body configuration.

The process of ego development and therefore distinction between self and not-self certainly would involve perceptive discrimination based on a receptive substrate, the component parts of which are intricately interacting anatomic constructs physiologically (and therefore dynamically) considered. This body image or ego is a continually developing process according to the well-known pleasure-pain and reality principles. It gains its maximum impetus in the initial stages and, after this beginning-acceleration, starts tapering off. It reaches a peak and eventually starts to drop, never under ordinary circumstances, getting to or falling below the original starting point. In disturbed states however, this can and does take place. The ego is considered by Federn as a "continuity, both lasting and recurring of the body and mental life relative to time, space and causality" (8). Further, he differentiates between body image, body scheme and bodily ego. The basic recognition of ones body is considered the body scheme and its various and varying alteration and position, mediating through proprioceptive senses is the body image. The bodily ego may be viewed as a combination of both of these and that its catalytic agent is a uniting cathexis. Thus, the bodily ego can be seen to be the body image plus the ego feeling or the "unified feeling of libido cathexis of motor and sensory apparatus" (8). The loss of ego boundary and dimensional alteration of the face and head affect the bodily ego feeling least and are due to a very strong libidinous cathexis of these anatomical parts. It is important to remember the difference of body scheme and bodily ego since there are times when they may operate independently and disproportionately to the degree that one may vanish before the other. Furthermore it should be noted that body image includes within it more than the concrete concept of body and might incorporate such extra personal objects as clothing, phantoms, etc. (10).

The ego not only consists of a bodily component but a mental one as well. This "mental ego feeling corresponding to inner perceptions is the first to be experienced by the child and ego feelings related to the body and to perceptions conceived through the body comes only gradually.... The fact that in everyone the subjective bodily feeling of the face (and its component parts) as least modified can be ac-

counted for by a strong libido cathexis just as a person with a marked degree of oral libido does not lose the bodily feeling of the mouth" (8). Similarly for each person each organ system and more specifically each individual organ have a certain quantum or cathected libido whose pattern and dynamic characteristics are singularly peculiar to it in its development, mobility or fluidity, and intensity.

But as is well known to those familiar with mental operations, the psyche's concept of anatomy is notoriously poor and mainly dependent on function. Its ideas of neuroanatomy are painfully inaccurate. As Freud pointed out in his discussion of the hysterics, "paralyses and other manifestations were as if anatomy were non-existent, or as if it had no knowledge of it" (17). This functional orientation has many determinants, including not only the internal physiology and psychology but also external interpersonal socio-cultural circumstances and temporal factors. The psyche "regards the organs according to the common popular meaning of their names. The leg is the leg up to its insertion into the hip. The arm is the upper extremity as mapped out by our clothing" (17). To most individuals the nose is for smell, the ears for hearing, the eyes for seeing, the mouth for drinking, eating, etc. Individually, these functions are ontogenically a much earlier acquisition than one's self-image concept, anatomically and psychologically. Further, one's self image may be viewed as a sum total of the individual interacting component parts. It is extremely important to recognize the interrelationships of these parts as, for example, concerns vision. Under ordinary circumstances, stereoscopic vision is dependent on binocular capacities. Gross visual acuity is an independent function in each eye. Therefore, when investigating the presence or absence of a phantom eye, one would probably get a negative response if the question were directed to gross vision since through the use of the intact eye compensation adequately maintains visual field and acuity function. However, a positive response would be forthcoming if the emphasis were placed on perspective perception. Because the ear lobe's role as a function of hearing is extremely small, a phantom after its loss would be somewhat more difficult to elicit and probably result in a small incidence.

Perhaps a clearer understanding of the meaning of the phantom symptom might be obtained through a study of its economy. By this we mean that operational level achieved in a psychological homeostatic equilibrium which attains the highest level of efficiency permitting the individual maximum ego integration and avoidance of conflict and consequent anxiety. This requires an intensive investigation into the dynamics of this system.

In the continuing alteration and modification of various factors within the psychological system in response to external changes, there are set up within that system certain characteristic modes of reaction which after constant repetition become increasingly channelized. Thus, on future exposure to the same or similar provocations, there is a facilitation of reaction to these which are then integrated within the ego components of the personality and which may be called memory traces or engrams. It can be readily seen that "increasing degrees of orientation in the present and in the immediate surroundings are brought about by a proportionate amount of orientation in the past" (28).

This process may be looked on as an associative one which, however, is continuously undergoing dissociative test situations. Usually the splitting off of fragments of the integrated body ego is temporary and quickly restored so that the wholeness is soon reintegrated by the conscious intact components of the ego. The principles of redintegration can well apply here. Hollingworth defines redintegration as "that process in which a part of a complex stimulus provokes the complete reaction that was previously made to the complex stimulus as a whole" (22). Though the pleasure-pain and reality principles are the determinants, the libido or psychic energy is the driving force which at any one time is proportionately distributed in the various component parts so that dynamic equilibrium is established, which in actuality is at any one time in a state of disequilibrium. A primary process takes place in that direction which is most direct, and it is only when interferences in either direction are met that detours and secondary processes are set up. Obviously, this must take place at the expense of decreased efficiency or increased expenditure of energy but always with the goal in mind of maintaining some intactness of the

ego. Some type of compromise formation is always employed, and its nature and degree can well serve as the indicator of the amount of maturation which has taken place within the personality.

Throughout life there is a constantly changing concentration of the psychic energy on various targets, both internal and external. This shifting fixation or cathectic process with ego feeling or object-libidinous attachment has been termed by Federn (8) as egotization and its splitting off as de-egotization. This process is in response to the demands of reality, and it should be pointed out that there is a definite difference between a sense of reality and reality testing. These are qualities inherent in the ego and, more particularly, within its boundary. This boundary is an ever changing one, and its vicissitudes determine the particular dissociative phase of the ego. Depersonalization and estrangement are manifestations of this changing ego boundary and, indeed, are extremely sensitive indicators of the ego's relationship to an alteration of and in accordance with reality demands. "In estrangement and depersonalization the perceptions, apperceptions, and/or proprioceptions may be changed, but intelligence and skills persist unaltered. They are both monosymptomatic ego disturbances. . . (and the latter) may be defined as a subjective experience of the disruption of one's ego and as an estrangement phenomenon of the ego. There is a definite alteration in self perception in both of these which concerns both body and mind. The patient with this symptom feels he accomplishes activity only with his bodily ego without the participation of his mental ego. However, the symptoms of depersonalization and estrangement are different in that in the former the core of the ego is deprived of the libido, whereas in the latter, only the ego boundaries have lost their libidinal component and again in the former there is a tendency of the person to live through past times as though they were in the present, and vice-versa" (8). Both the phantom phenomenon and deja vu are symptomatic manifestations of this process. "The condition of sleep, like illness, implies a narcissistic withdrawal of the libido away from the attachment back to the subject's own person" (15). In falling asleep, while the mental ego may remain intact, the bodily ego vanishes though it can be recalled by the mental ego. Thus depersonalization and sleep seem to be diametrically opposite processes in this regard. In extreme mental fatigue, however, there is a persistent diminution of the mental ego.

In the course of daily activities there is within the ego a sensitive balance of organ libidinal cathexis such that the individual is unaware of the very existence of any individual organ. However, as has been pointed out frequently in psychoanalytic literature, in the diseased state there is a reorientation of the libidinal distribution with the greatest concentration being centered on the offending organ. In this pathoneurotic state (according to Ferenczi's term) (11), it is almost as though the ego was particularly aware of the distorted stage and was attempting to reestablish the homeostatic equilibrium. As Ferenczi so clearly pointed out (11), there is a marked regression into narcissism when there is injury to some body area which is particularly charged with libido and with which the entire ego identifies. When the injury occurs to an organ with a particularly high quantum of libidinous investment, there is naturally to be expected a greater disturbance of ego integration. Ferenczi further stated, "identification of the whole ego with parts of the face is common to all mankind . . . the eye is one of the bodily organs most powerfully charged with libido, as is shown not only by psycho-analysis of the neuroses, but also by the wealth of folklore relating to the value of the eye. It is comprehensible that the loss of an eye or the risk of this should sympathetically involve the whole ego or give rise to a narcissistic disease—neurosis" (11).

The organizational equilibrium of psychological systems may be visualized as following quite closely Hughlings Jackson's Law of Evolution and Dissolution of the Nervous System (23). According to this concept, the later the acquisition and the more complex the memory, the more the susceptibility to maladjustment or distortion, the greater the degree of impairment and the longer the duration of the disturbance. The converse is true for the earlier functions and as Federn stated "the bodily ego feeling relating to the face and the head remains unaffected by these modifications of loss

of ego boundary alteration and dimensional alteration the longest of all" (8). Thus, if the notion of psycho-sexual development is accepted, it can be seen that the application of this principle to the understanding of the phantom face should be observed not less but more frequently than phantom limbs. Further, phantoms may be viewed as a continuously operating orthriogenetic process whereby there is an ego orientation to reality undergoing a "materialization phenomenon", which basically means a fantasy reconstruction of the lost object using the method of denial with "reversal of the real facts into their opposite" (12). This redintegrative reegotization of the phantom then can be considered the antithesis of, though dynamically closely related to, depersonalization and feelings of estrangement. The individual in his inability to surrender to the reality of the loss and accept less than totality of the integrated body configuration uses intense denial with a reaction formation restitutive reorganization of ego perception of the self image.

Certainly, more detailed investigation must be done to substantiate these initial impressions, and a greater variety and a larger series of cases are needed. This would require studying incidences in both sexes, amputation of various anatomical features and for various reasons. It would be extremely elucidating if these studies could be made to include the premorbid stage of each case.

In any event, on the basis of this preliminary study it is the author's opinion that phantoms of facial parts do exist. Furthermore, it is strongly suspected that the frequency is at least as high as limb phantoms. Certainly, phantom syndrome of facial parts is in excellent accord with basic psychoanalytic principles.

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BIBLIOGRAPHY

1. Abel, T. M.: Facial Disfigurement. *Psychological Aspects of Physical Disability*, pp. 112–123. J. F. Garrett, Editor, Federal Security Agency, Office of Vocational Rehabilitation, Rehabilitation Service, Series Number 210, Washington 25, D. C.
2. Abel, T. M.: Figure drawings in facial disfigurement. *Am. J. Orthopsychial., 23:* 253–261, 1953.
3. Baker, W. Y., and Smith, L. H.: Facial disfigurement and personality. *J. A. M. A., 112:* 301, 1939.
4. Barsky, A. J.: *The Principles and Practices of Plastic Surgery*. Baltimore: The Williams and Wilkins Company, 1950.
5. Berndorfer, A.: Plastic Surgery, Physiognomy, and Psychoanalysis. *Plastic & Reconstructive Surg. 4:* 453–458, 1949.
6. Dembo, T. *et al.:* Acceptance of Loss—Amputation. *Psychological Aspects of Physical Disability*, pp. 89–96. J. F. Garrett, Editor, Federal Security Agency, Office of Vocational Rehabilitation, Rehabilitation Service, Series Number 210, Washington 25, D. C.
7. Deutsch, F., and Murphy, W. F.: *The Clinical Interview*. Volume 1, Diagnosis, Chapter 8, pp. 204–256. New York: International Universities Press, Incorporated.
8. Federn, P.: *Ego Psychology and the Psychoses*. Editor: E. Weiss. New York: Basic Books, Incorporated, 1952.
9. Fenichel, O.: *The Collected Papers of Otto Fenichel*, First Series. Editors: H. Fenichel and D. Rapaport. New York: W. W. Norton & Company, Incorporated, 1953.
10. Fenichel, O.: *The Psycho-analytic Theory of Neuroses*. New York: W. W. Norton & Company, 1945.
11. Ferenczi, S.: *The Theory and Technique of Psychoanalyses*. London: Hogarth Press Limited, 1950.
12. Freud, A.: *The Ego and Mechanisms of Defence*. New York: International Universities Press, 1946.
13. Freud, S.: *A Note on the Unconscious in Psychoanalyses*, Collected Papers, Volume 4, pp. 22–29. London: Hogarth Press, 1949.
14. Freud, S.: *Formulations Regarding the Two Principles in Mental Functioning*, Collected Papers, Volume 4, pp. 12–21. London: Hogarth Press Limited, 1949.
15. Freud, S.: *On Narcissism: An Introduction*, Collected Papers, Volume 4, pp. 30–59. London: Hogarth Press Limited, 1949.
16. Freud, S.: *Repression*, Collected Papers, Volume 4, pp. 84–97. London: Hogarth Press, 1949.
17. Freud, S.: *Some Points in a Comparative Study of Organic and Historical Paralyses*, Collected Papers, Volume 1, pp. 42–58. London: Hogarth Press Limited, 1949.
18. Freud, S.: *The Unconscious*, Collected Papers, Volume 4, pp. 98–136. London: Hogarth Press Limited, 1949.
19. Gallinek, A.: The phantom limb: Its origin and relation to the hallucinations of psychotic state. *Am. J. Psychial., 6:* 1939.
20. Hill, G., and Silver, G. A.: Psychodynamic and esthetic motivations for plastic surgery. *Psychosomatic Med., 6:* 345–355, 1950.
21. Hoffman, J.: Phantom limb syndrome. A critical review of the literature. *J. Nerv. & Ment. Dis., 119:* 261–270, 1954.
22. Hollingworth, H. L.: *The Psychology of Functional Neuroses*. New York: D. Appleton & Company, 1920.
23. Jackson, J. H.: The Croonian Lectures on the evolution and dissolution of the nervous system, *Brit.*

Med. J., I (1884), 591, 660, 703, (Lectures I, II, III) quoted by Rosett.

24. Lowenfeld, B.: The Blind. *Psychological Aspects of Physical Disability*, pp. 179–195. J. F. Garrett, Editor, Federal Security Agency, Office of Vocational Rehabilitation, Rehabilitation Service, Series Number 210, Washington 25, D. C.
25. MacGregor, F. *et al.*: *Facial Deformities and Plastic Surgery—A Psychological Study*. Springfield, Ill.: Charles C Thomas, 1953.
26. Menninger, K. A.: *Psychiatric Aspects of Physical Disability*, pp. 8–17. J. F. Garrett, Editor, Federal Security Agency, Office of Vocational Rehabilitation, Rehabilitation Service, Series Number 210, Washington 25, D. C.
27. Rosen, V. H.: The role of denial in acute post operative affective reactions following removal of body parts. *Psychosomatic Med., 12:* 1950.
28. Rossett, J.: *The Mechanism of Thought, Imagery and Hallucination*. New York: Columbia University Press, 1939.
29. Schilder, P.: *Medical Psychology*. Editor: D. Rapaport. New York: International Universities Press, Incorporated, 1953.
30. Schilder, P.: *The Image and Appearance of the Human Body*. New York: International Universities Press Incorporated, 1950.
31. Updegraff, H. L., and Menninger, K. A.: Some Psycho-analytic Aspects of Plastic Surgery. *Am. J. Surg., 25:* 554–558, 1934.
32. Young, F.: The Surgical repair of nasal deformities. *J. Plastic & Reconstructive Surg., 4:* 59–92, 1949.

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THE USE OF DEPENDENCE FOR PREDICTING PSYCHOGENIC INVALIDISM FOLLOWING RADICAL MASTECTOMY[1]

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It was the purpose of this investigation to determine the relationship of the personality factor of dependence to psychogenic invalidism in women after radical mastectomy for breast cancer. The problem of this study was essentially predictive and sought to eliminate the methodologic limitations of previous investigations concerning emotional reactions to surgery. In the past, individual clinical experience provided the primary basis for published recommendations (8, 9, 20) regarding the etiology and management of post-operative emotional disorders. Although commendable in many ways, these accounts are subject to the vagaries and distortions of individual experience and are unsupported by research findings. Where actual research has been conducted, post-operative psychoses held the focus of interest (1) with attempts to reconstruct contributory factors after the psychosis was manifested.

Before the turn of the century, Picque (26) recognized the need for predictive studies and suggested that exploration of personality factors before operation would permit reasonable predictions of post-operative emotional responses. In 1930, McGraw (21) took a similar stand, pointing out that emotional disorders after surgery indicated a breakdown in the adaptive capacity of the organism. He stated that breakdowns occur when the individual is confronted by special stress and advocated further efforts to assess the probable adaptability of individuals faced with the stress of surgery. More recently, a noted surgeon (4), aware of the psychological factors influencing the course of surgical patients, called for adequate research: "A study of conditions before and after operation by methods known only to the experienced psychologist would undoubtedly advance our knowledge of both psychiatry and surgery."

Efforts to establish criteria for the prediction of post-operative emotional responses were clear in the investigations of Lindemann (19) and Schneider, Gray, and Culmer (30). These investigators sought to avoid the pitfalls of *ex post facto* research.[3] Lindemann studied 51 women, 20–55 years of age, prior to major abdominal surgery. After operation, he re-examined 40 of the patients who presented no physical complications and whose convalescence appeared uneventful. He found that 25 of the patients re-examined evidenced no change in psychiatric status, but that the remaining 15 were seriously depressed, sleepless, agitated or restless for periods from 3 days post-operative to as long as 3 months. He pointed out that his method illustrated the need for detailed pre-operative study before reliable predictions of post-operative psychiatric course are possible.

Recently, Schneider, Gray, and Culmer studied the correlation between pre-operative psychometric findings and recovery after surgery. In their study, undertaken to develop a predictive procedure, the Minnesota Multiphonic Personality Inventory was administered to 275 patients scheduled for various types of surgery. In addition to the MMPI, the patients were interviewed for socio-economic data, and the Schneider-Gray Inventory was administered. The questionnaire, designed for use in the study, elicited the patient's attitudes toward physicians, hospitals and surgery. Post-operative evaluation consisted of a recovery progress report submitted by the surgeon after each clinic follow-up visit and a questionnaire completed by a close relative or friend report-

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[3] This term refers to the study of acute post-operative emotional reactions *after* they are manifested. An effort is then made to distinguish contributory pre-morbid (usually pre-operative) factors by reconstruction, retrospective analysis and inferential reasoning.

ing the patient's progress on a four-point scale from "very well" to "very poorly." The authors found that patients who had previous multiple surgery showed a significant correlation between pre-operative data and the recovery data. Also, they found 14 items of the Schneider-Gray Inventory that were significantly related to the recovery reports by families.

Ruesch (28) studied the psychological factors in cases of prolonged convalescence after chronic illness. He found that in a large proportion of cases dependency was the primary defense mechanism, and that women more frequently than men manifest dependency conflicts following a siege of serious illness. Furthermore, he noted that invalid reactions to physical illness and surgery often are based almost entirely upon psychogenic factors. A study of the psychological impact of the dry colostomy (33) also emphasized the role of post-operative psychogenic invalidism in patients.

The relationship between dependency and psychogenic invalidism established by previous investigators indicated that the personality factor of dependence could be used predictively with regard to post-operative psychogenic invalidism. In addition, the qualitative significance of dependence in the psychosexual development of women also sustained its use as the personality variable of choice for the prediction of psychogenic invalid reactions to radical mastectomy.

From its inception, dynamic psychology focused upon early mother-child relations. There is wide agreement that this relationship is critically important in emotional development and is a basic factor in dependence. It has been pointed out that dependence in early infancy is realistically related to biological helplessness, but that the use of dependence as a primary technique of adaptation in adulthood is a reflection of psychological need rather than biological necessity (16). Jones (15), on the other hand, expressed the view that biological factors are less a consideration in infancy than is the fact that dependence is related to the need for love and that "it is a characteristic phenomenon of the oedipus complex of infancy." While Levy (18) defined maternal overprotection as the primary factor in excessive childhood dependence, another (32) has emphasized that any number of disturbed relationships with the mother can result in dependency problems. Deutsch (6) viewed female homosexuality as a pathological extreme of excessive dependence, reflecting a recapitulation of an early mother-daughter relationship characterized by dependency and hostility.

Using dependence as the predictive variable in a study of responses to breast amputation takes on added significance when one considers the role of the breast in female psychosexual development, especially during pubescence. Adolescence is the period when the maturing girl makes desperate efforts to liberate herself from infantile dependencies.

> If the girl does not solve the problem of adolescence, she remains during this period and likewise later as a maturing or mature woman the child she was during pre-puberty, continually aggressive and nervously struggling against this tie with her mother, developing various symptoms in connection with her conflict and persisting in a completely passive dependence (7, p. 118).

Maturity, optimum functioning efficiency and ability for independent action are possible only when there has been a satisfactory resolution of dependency conflicts and liberation from maternal control during puberty.

The pubescent girl, moreover, is confronted with the necessity of adaptation to striking physical changes such as the onset of menarche and breast development. A fusion frequently occurs between the problems inherent in resolving infantile needs and the problems created by changing physical characteristics (3). A mother's reluctance to accept her daughter's achievement of independence may adversely influence the girl's perception of her changing body. The daughter may interpret maternal resistance to independence as disapproval of developing female physical characteristics, thus engendering or increasing anxiety and guilt. Menninger (23) found that a large percentage of pubescent girls are mortified and guilt-ridden about their breasts, many of them binding their breasts to conceal them or to prevent further development. Attempts to resolve dependency conflicts with the mother usually occur during this period and may have a profound effect upon subsequent adult feminine functioning.

Dependence can be regarded as a personality

component which results in the real or fantasied solicitation of support or protection from individuals regarded as nurturant or powerful. In this study, the degree to which it was present was determined by the extent to which a patient was unable to free herself from maternal control. A fundamental hypothesis of this investigation was that dependent women respond to radical mastectomy with a prolonged period of depression, an exaggerated sense of weakness, withdrawal from social participation, and a marked disruption of usual functioning. On the other hand, independent or self-reliant women respond to radical mastectomy with a less intense and shorter period of depression, less intense sense of weakness, a shorter period of withdrawal from social participation, and manifest a more rapid resumption of usual functioning.

Sample and Method

Twenty white female patients in the Breast Clinic of the Memorial Hospital were selected for study on the basis of the following criteria: 1) a primary operable carcinoma of the breast with no other disease; 2) absence of menopausal symptoms; 3) no history of previous surgery; and, 4) no history of psychiatric consultation. The patients selected ranged in age frum 28 to 58 years with a mean age of 42.4 years and a median age of 43.5 years.[4]

Thirteen of the patients were Roman Catholics, six were Hebrews and one was a Protestant. Fifteen were married, one single, three divorced and one widowed. The United States was the birthplace of thirteen, four were born in Italy, and one each in Poland, Germany and Hungary. Education was distributed as follows: four patients did not complete elementary school and three attended college. Of the others, ten patients had attended or completed high school and two had attended a business college after elementary school. Fifteen patients were housewives, two were embroiderers, and the others were a machine operator, a retail saleslady and a record clerk. The husbands of these patients were skilled workers primarily; none of them was a professional or business owner.

Since the problem of this study was essentially predictive, psychological procedures were selected which are assumed valid for revealing personality differences and for identifying dependence. They were the Rorschach Test, modified Thematic Apperception Test and a specially designed focused interview.

The psychological literature contains reports of the exhaustive work done on Rorschach validation as an instrument for personality evaluation. Case study data and psychiatric diagnoses were the usual experimental criteria employed in these studies. The Rorschach Test has been used in predictive studies as well. Morris (24), for example, utilized the Rorschach as a predictive technique in a study in which dependence was one of 42 personality variables. In his study, dependence was one of the 17 variables which showed a significant correlation with the criteria. In the light of past experience and research with the Rorschach, it appeared particularly suitable for use as a predictive technique in the present study.

Similarly, the Thematic Apperception Test has established itself as an instrument that "yields statistically and clinically significant results in the prediction of behavior and personality" (14, p. 35). It appeared particularly valuable, for as Sontag *et al.* have pointed out:

> Analysis of Thematic Apperception Test psychiatric interviews may be structured to 1) measure the degree of resolution of infantile dependency, 2) delineate the nature of the devices an individual uses to attempt to satisfy love needs, 3) appraise the nature and adequacy of the ego defenses against anxiety or frustration of infantile dependency needs or adult ego needs (31, p. 537).

Since "the most common direct modification of the TAT is in shortening the test by reducing the number of stimulus-pictures used" (2), 10 of the series regarded as most relevant to the hypothesis of this study were used. They were as follows: 2, 3 GF, 4, 5, 6 GF, 6 BM, 7 GF, 9 GF, 10 and 12 F. The method of administering the test was essentially the same as the procedure set forth in Murray's manual (25). If the responses were ambiguous, lacked structure or were grossly impoverished, the investigator encouraged elaboration by nonsuggestive inquiry.

[4] During the three year period, 1946–1948, 67 per cent of all white, clinic radical mastectomy patients at Memorial Hospital were within this age range. The sample used in this investigation, therefore, is representative of this type of patient ordinarily seen at Memorial Hospital (22).

The predictive value of brief psychiatric interviews has been established in other studies (5, 35). A predictive interview procedure was designed for this study which focused on female psychosexual development and which was calculated to facilitate judgments of the extent of dependence in the personalities of the subjects. After Finesinger (10), the method encourages the patient to "communicate in meaningful areas" allowing free expression yet employing verbal and non-verbal cues by the interviewer to focus the material. In the present study, the subjects were "focused" on particular life experiences (table 1) associated with the hypothesis. At all times the interview form was used as a guide rather than as a rigid questionnaire. The interview was planned and consistent, however, thus insuring exploration of comparable aspects of development with each subject.

TABLE 1.—Pre-Operative Focused Interview Guide

1. Personal history face sheet.
2. Menstruation
   a. Menarche—age at onset—attitudes and feelings.
   b. Cycle—regularity, reactions, how referred to.
   c. Menopause—age, symptoms and feelings.
3. Early feelings about development of secondary sex characteristics. Attitudes and fantasies in this area.
4. Past and present attitudes toward breasts. Meaning and importance of breasts.
5. Sex knowledge. Early instruction and feeling concerning sexual activity.
6. Early and pre-marital heterosexual activity. Interests and prohibitions in dating. Family attitude toward heterosexual contacts.
7. Occupational history. Attitudes toward work and feelings regarding work and/or housework.
8. Marital relationship
   a. Parents' feeling concerning husband before and after marriage.
   b. Length of courtship.
   c. Sexual function.
9. Pregnancy and delivery. Feelings concerning childbirth. Were children planned? Abortions?
10. Self-concept.
11. Feelings regarding feminine activity.
12. Past and present sleeping pattern.
13. Past and present eating pattern.
14. Dreams—past and present.
15. Attitudes toward parental figures.
16. Significant stress situations during life and reactions to them, (e.g., death, injury, sickness, financial, etc.).
17. Feelings regarding impending surgery. Attitudes regarding operation. Meaning of the operation.

TABLE 2.—Post-Operative Focused Interview Guide

1. Feelings just prior to surgery. Feelings upon anesthetization.
2. Feelings immediately after surgery. Reaction when learned of the radical nature of the surgery. How learned.
3. Immediate pre-operative sleeping pattern.
4. Immediate post-operative sleeping pattern.
5. Immediate pre-operative eating pattern.
6. Immediate post-operative eating pattern.
7. Dreams. The night before surgery and any dreams since the operation.
8. Activity upon arrival home. Who helped? How?
9. How long a convalescence is regarded by the patient as necessary.
10. Social relatedness. When commenced. Attitudes toward people.
11. Self-concept. Note patient's reference to change in concept.
12. Mood since operation.
13. Sexual activity. Frequency and when resumed. Attitudes toward sexual function and desire.
14. Husband's general and specific attitude as depicted by patient.
15. Attitudes toward body. Feelings about others "knowing".
16. Feelings about recurrence, physical complaints and complications.
17. Characterization of other patients on the ward and in the clinic.

While three predictive techniques (Rorschach, TAT and interview) were employed, only one criterion technique was used. The criterion technique was a post-operative interview designed to evaluate psychogenic invalidism (table 2). The findings of Ruesch (28) and Sutherland *et al.* (33) were used to establish the criteria of invalidism: depression, sense of weakness, social withdrawal and resumption of usual motor activity. The method followed in conducting the post-operative criterion interview was the same as the one employed in the pre-operative predictive interview.

The patients were selected for study on the day that the diagnosis of breast cancer was established. The author administered the predictive psychological tests and conducted the predictive interview in uniform sequence with each patient. If the procedures were questioned, they were interpreted as a routine but important phase of pre-operative medical procedure as yet unavailable to all patients due to staff shortage. This interpretation usually reassured the patient and tended to improve

motivation and cooperation. Furthermore, consistent with hospital policy, no effort was made to inform patients of the probability of radical mastectomy. Nevertheless, with knowledge that breast surgery would be performed, the possibility of mastectomy was recognized by a number of patients either because of past experiences with friends or relatives or because of their own anxious expectations.

Each patient was hospitalized for 6 days post-operatively. During hospitalization each patient's manifest behavior was noted on a brief form by the recreational therapist usually present on the ward. Not less than 6 weeks nor more than 10 weeks after discharge, each patient was again interviewed for the purpose of qualitatively establishing the invalid status as defined by the criterion interview.

Treatment of the Data

Initially, interpretations of the tests and the predictive interviews were obtained from two clinical psychologists and one psychiatrist who had no prior connection with this study. One psychologist interpreted the Rorschach protocols; the other evaluated the TAT records, and the psychiatrist examined the interview data. The two psychologists, who had completed 3 years of graduate training and had at least 5 years of professional test experience, were assumed to be skilled and qualified. The psychiatrist had completed psychiatric and psychotherapeutic training and was assumed qualified to interpret interview data with regard to the predictive variable.

The predictive test and interview data were evaluated to provide some estimate of the quality of dependence in each patient's personality. To facilitate evaluation of dependence each predictive technique "analyst" was provided with the operational definition of dependence.[5] Although dependence is frequently evaluated by the TAT and Rorschach Test, there are no universally agreed test "signs" for this variable. The test analysts were not rigidly bound by the operational definition of dependence but were permitted to employ test criteria of the variable developed in the course of their own clinical experience as well.[6] Each analyst then wrote a summary of his interpretation of dependence for every record evaluated by him.

Two judges independently rank ordered the interpretative summaries for each of the predictive techniques for the extent of dependence. The order of rank was from most dependent to least dependent, that is, the patient judged most dependent on the basis of the interpretative summary was ranked 1 and the patient judged least dependent was ranked 20.

The post-operative (criterion) interview data were treated in a similar fashion. The data were submitted to a skilled and qualified psychotherapist, who had no other association with the study, for his evaluation of invalidism. He evaluated the data to determine the quality of depression, weakness, social participation and motor activity and then wrote a summary of interpretation for each patient's record. Two judges independently rank ordered the summaries for the extent of invalidism, ranking the most invalided as 1 and the least invalided as 20.

The utilization of two judges for each predictive technique and two judges for the criterion technique provided an estimate of the reliability of the rankings. In order to increase the estimate of reliability, the ranks of the two judges for each technique were pooled (13).

A further estimate of increased reliability was provided by application of the Spearman-Brown formula. No attempt was made to transform the ranking into scale values since there is no evidence that the personality variable of dependence is normally distributed in the general population—a necessary assumption before such transformations are possible. Were the judgments concerned with intelligence or some other attribute, such an assumption would be tenable. Furthermore, the data of this investigation were qualitative, thus precluding precise measurement. The use of the rank order method "does not require the assumption of normality of the data which underlies such procedures as the analysis of

[5] In this study dependence is defined as a basic personality component expressed in the solicitation of support and protection from those regarded as powerful and nurturant. Its presence is further defined by the extent to which a patient has been unable to free herself from maternal control.

[6] Requiring the analysts to conform to a given system of analysis would have impaired their clinical skills and adversely influenced their interpretations since "in the case of most clinical techniques, the clinician himself is part of the psychological test," (17).

TABLE 3.—EXTENT OF AGREEMENT BETWEEN TWO JUDGES RANKING THE INTERPRETIVE SUMMARIES OF EACH TECHNIQUE

Technique	r	Spearman-Brown
Rorschach Test	.832	.908
Pre-operative interview	.680	.810
Thematic Apperception Test	.761	.864
Post-operative interview	.965	.982

TABLE 4.—CORRELATIONS AMONG THE POOLED DEPENDENCE RANKINGS OF THE PRE-OPERATIVE TECHNIQUES

Rank Order Correlations between	Rank Correlation Coefficient*
Rorschach and TAT	.155
TAT and pre-operative interview	.023
Pre-operative interview and Rorschach	.118

* .05 Level of Significance—.377.

variance" (34); therefore, the method is most useful in situations where data are not susceptible to exact measurement.

The results of estimating the extent of agreement between the two judges ranking the interpretative summaries for each technique are presented in table 3. It is apparent that there was a high degree of agreement, at the .01 per cent level of significance, between the two judges for each technique. Further rank-order correlations were computed to determine the relationships among the pooled dependence ranks of each pre-operative technique. The nature of the relationships among the three pre-operative techniques (table 4) revealed that although the techniques were reliably judged, they lacked communality with respect to the personality factor of dependence. The final stage in statistical analysis was to determine the relationship between each pre-operative technique and the post-operative interview. The resulting correlations indicated that there was a low negative correlation between the pre-operative tests and the post-operative interview. However, the correlation between the pooled dependence rankings of the pre-operative interview and the invalidism rankings of post-operative interview was significant at the .05 per cent level and almost significant at the .01 per cent level.

INTERPRETATION OF FINDINGS

Although the interpretations of the techniques employed in this study were reliably ranked, statistical analysis of the relationships among the three predictive techniques revealed an absence of communality with respect to the personality factor of dependence. Possible explanations for this finding were as follows:

1. While the projective tests employed in this study are considered valid for the identification of personality components, the nature of the stress situation in which they were administered may have caused other personality factors (such as anxiety and defenses in response to the stress) to obscure the single factor relevant to the hypothesis. Other investigators have noted the impact of unusual environmental conditions upon projective test responses (27).

2. It is possible that overt adaptive patterns in everyday living are not reflected in projective tests and that the strength of these tests rests in their ability to reveal fantasies and inner psychodynamics. Indeed, the same basic personality factor may be expressed in diametrically opposed adaptive patterns. For example, as Sapirstein (29) has pointed out, for one individual dependency conflicts may result in a compulsive insistence upon independent action, even when such independence is completely inappropriate. In contrast, a second individual may constantly seek support from nurturant figures even under the mildest circumstances. Consequently, it appears that the pre-operative interview which was concerned with specific life adaptations, the Rorschach Test which assessed basic personality dynamics, and the TAT which uncovered fantasy were all evaluating the same personality variable but from different frames of reference. Such interpretation is in agreement with the theoretical position of Grinker and Spiegel (12) who believe that there is a dynamic interplay between personality, life adaptation, previous stress and current stress. Furthermore, Goldfarb emphasized that the Rorschach Test can be profitably used to test hypotheses regarding certain traits, but with the following qualification:

> Overt behavior is predicted with difficulty . . . the most conspicuous tendencies tend to dominate the test . . . the test gives a cross-sectional picture of the individual at a given moment. He is not seen in the process of change and development (11, p. 327).

A similar limitation in the TAT was noted by Murray who considered that the psychologist can best understand personality by determining "the characteristics of manifest behavior in conjunction with the TAT findings" (25, p. 16).

3. The attitudes of the patients toward the various techniques employed in this research may have varied considerably. Patients are frequently very anxious about any hospital procedure not completely understood by them. A threatening situation which stimulates an alertness to the possibility of injury breeds a strong desire to become familiar with every aspect of the experience. By their very nature, projective tests are difficult for the average person to understand, even when they are administered in situations devoid of danger. It is reasonable to infer, therefore, that the unfamiliar and unstructured projective tests increased perceptual distortions and the tension which already existed, while motivation, association, and fantasy activity were decreased. The pre-operative (predictive) focused interview, on the other hand, was concerned with life history data and, thus, was usually identified by the patient as medically pertinent. In fact, there were many spontaneous comments about how much more exhaustive the interview was than any other "medical history" taken up to that time.

Only the focused interview, of the three predictive techniques, correlated significantly with the criterion (invalidism) technique at five per cent level of significance (table 5). The Rorschach Test and TAT were not significantly correlated. There are a number of possible explanations for this:

1. Evaluations of dependence are contingent on a study of early childhood experiences and long-term adaptations in living. Projective tests, when administered under the stressful circumstances existing at the time of their use in this investigation, may be unable to provide with consistency the data necessary for the evaluation of dependence. Although the tests permitted inferences about the variable in some cases, the interview, focused on early life experiences and adaptive patterns, could identify the variable in a larger number of cases and, consequently, endowed the interview with great predictability.

2. The analysts of the projective tests were experienced and skilful, and a technical assumption underlying this study provided that skilled interpreters were capable of identifying and evaluating dependence on the tests. Although it is possible that the analysts were in error, there is sufficient evidence that an increase in the number of analysts does not eliminate such error in psychological research. Morris (24) utilized six test analysts in his study and found that despite similar skilfulness interpreters tended to be "good" or "bad," dependent upon the personality factor being analyzed and upon differences in backgrounds among the analysts.

3. Due to individual variations in the responses of the patients to the interview, life history data were not complete for some. As a result, the patients for whom less information was available were necessarily ranked less precisely by the judges. However, even with somewhat incomplete interview data for some of the patients, the relationship between the pre-operative and post-operative interview data was significantly high at the five per cent level. It appears that if more complete life history material was available, the relationship between the two interviews would have increased still further.

TABLE 5.—Correlations between the Pooled Dependence Rankings of Each Pre-Operative Technique and the Pooled Invalidism Rankings of the Post-Operative Interview Data

Rank Order Correlations between	Rank Correlation Coefficient*
Rorschach and post-operative interview	.198
TAT and post-operative interview	.134
Pre-operative interview and post-operative interview	.495

* .05 Level of Significance—.377.

Discussion

Sutherland and his associates (33) pointed out that psychologically determined invalid reactions to surgery are a growing problem in medicine. Although this investigation has not provided a solution to the problem, it has demonstrated the value of employing pre-operative personality study for the prediction of post-operative invalidism. Picque (26), before the turn of the century, and McGraw (21), more recently, emphasized that only with

thorough knowledge of a patient's personality is it possible to predict post-operative emotional reactions. Previous investigators have been primarily concerned with post-operative psychoses, thus requiring retrospective analyses and reconstruction to determine the role of contributory personality factors. However, other investigators, notably Lindemann (19) and Schneider *et al.* (30), recognized the inherent weakness in such an approach and specifically designed their studies to permit pre-operative evaluation of randomly selected surgical patients. In addition to the predictive possibilities in their research designs, they also emphasized that such an approach to patients provides a unique source of psychodynamic material.

The data of the present investigation have provided an estimate of the relationship between a single personality variable to post-operative invalidism in a group of patients who underwent a uniform surgical procedure. Although a rather small sample of patients was studied, there is a strong suggestion of the advisability of tracing personality through the life span of the individual before effective prediction of behavior is possible. The development of personality is a process of integrations and adaptations in living and not merely an aggregate of unrelated facts. Consequently, an individual's response to a specific stress experience can be best determined by an assessment of lifelong adaptations. Of course, there are specific adaptive techniques employed which are more pertinent to some types of stress than to others. In this study, psychological integration in feminine development was used to delineate the response of women to the defeminizing stress of breast amputation. The most effective method of determining the sequence of life adaptations in feminine development was by interviews which focused upon psychosexual development.

Although projective tests are very useful in studying character structure, their primary function appears to be the elaboration of dynamic, unconscious conflicts underlying behavior. However, the same dynamic conflict in two different individuals often results in completely dissimilar adaptive patterns. It appears, therefore, that psychological test data alone may not provide sufficient understanding of adaptive patterns since they primarily afford a glimpse into underlying psychodynamic conflicts. In this investigation the insights provided by focused interview were more predictive of reaction to the stress of radical mastectomy than the results of the Rorschach Test and TAT. But it is entirely possible that the use of other personality variables for the purpose of prediction would demonstrate that projective tests have greater value.

Summary

It was the purpose of this investigation to determine the relationship of the personality variable of dependence to psychogenic invalidism in women following radical mastectomy (removal of a breast, pectorales muscles and axillary contents). The subjects were twenty white females diagnosed as having cancer of the breast at Memorial Hospital, New York City. They were between twenty-eight and fifty-seven years of age, free of menopausal symptoms or other disease, and had no psychiatric or surgical histories. Based on these delimitations, each subject was selected on the day that the cancer was diagnosed, and the necessity for radical mastectomy determined.

The Rorschach Test, Thematic Apperception Test, and a focused interview specifically designed for this study were employed to evaluate the personality factor of dependence. The tests were administered and the interview conducted by the investigator in uniform sequence prior to operation. During the six-day post-operative hospitalization period, each subject was observed and her activity patterns noted on a specially constructed form. Not less than six weeks nor more than ten weeks after discharge from the hospital, a focused interview was conducted with each subject to determine emotional reactions and everyday activity patterns in diverse areas of living, such as housework, social, recreational and sexual activities.

Statistical analysis of the data by the rank-order method revealed that judges can reliably rank the extent of dependence based on the Rorschach Test, Thematic Apperception Test and focused interview interpretations. Analysis revealed a lack of communality among the three pre-operative techniques with regard to dependence. The extent of dependence determined by the Rorschach Test was related,

but not significantly, to the extent of invalidism determined by the post-operative interview. However, the extent of dependence determined by the pre-operative focused interview was related to the extent of invalidism at the five per cent level of significance.

It was concluded that there was a demonstrable relationship between the extent of dependence and the extent of psychogenic invalidism following radical mastectomy. However, although dependence could be determined on the basis of all the pre-operative techniques, only the evaluations derived from the pre-operative focused interview were significantly related to the criterion of invalidism. Finally, there was a suggestion that future refinements in the focused interview method could enable accurate pre-operative predictions of psychogenic invalidism following radical mastectomy.

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BIBLIOGRAPHY

1. Abeles, M. M.: Postoperative psychoses. *Am. J. Psychiat., 94:* 1187–1203, 1938.
2. Bell, J. E.: *Projective Techniques:* New York: Longmans, Green and Company, 1948.
3. Benedek, T.: Psychosexual function in women. In *Encyclopedia of Psychology.* New York: Citadel Press, 1946.
4. Brooks, B.: Psychosomatic surgery. *Ann. Surg., 110:* 288–299, 1944.
5. Deemer, W. L., and Rafferty, J. A.: Experimental evaluation of the psychiatric interview for prediction of success in pilot training. *J. Aviation Med., 20:* 238–250, 1949.
6. Deutsch, H.: On female homosexuality. *Psychoanalyt. Quart., 1:* 484–510, 1932.
7. Deutsch, H.: *Psychology of Women,* Vol. I. New York: Grune and Stratton, 1944.
8. Deutsch, H.: Some psychoanalytic observations in surgery. *Psychosomatic Med., 4:* 105–115, 1942.
9. Ficarra, B. J.: *Psychosomatic Aspects of Surgery.* New York: Forben Press, 1951.
10. Finesinger, J. E.: Psychiatric interviewing. *Am. J. Psychiat., 105:* 187–195, 1948.
11. Goldfarb, W.: The Rorschach experiment. In *The Mark of Oppression.* Editors: A. Kardiner and L. Ovesey. New York: W. W. Norton and Company, 1951.
12. Grinker, R., and Spiegel, R.: *Men Under Stress.* Philadelphia: Blakeston, 1945.
13. Guilford, J. P.: *Psychometric Methods.* New York: McGraw Hill, 1936.
14. Hartman, A. A.: An experimental examination of the thermatic apperception test in clinical diagnosis. *Psychological Monographs, 63:* 1–48, 1949.
15. Jones, E.: *Papers on Psychoanalysis.* New York: William Woods and Company, 1923.
16. Kardiner, A.: *The Individual and His Society.* New York: Columbia University Press, 1939.
17. Kelley, E. L.: The prediction of success in clinical psychology. In *Relation of Psychological Tests to Psychiatry.* Editors: P. Hoch and J. Zubin. New York: Grune and Stratton, 1951.
18. Levy, D. M.: Maternal overprotection. *Psychiatry, 1:* 561–591, 1938.
19. Lindemann, E.: Observations on psychiatric sequelae to surgical operations in women. *Am. J. Psychiat., 98:* 132–139, 1941.
20. Lipkin, M., and Joseph, E.: Some psychosomatic aspects of the management of surgical patients. *Surgery, 25:* 268–275, 1949.
21. McGraw, R. B.: Postoperative emotional disorders. *Bulletin of the New York Academy of Medicine, 6:* 179–188, 1930.
22. Memorial Hospital, Department of Statistics.
23. Menninger, K. A.: Somatic correlations with the unconscious repudiation of femininity in women. *J. Nerv. & Ment. Dis., 89:* 514–527, 1939.
24. Morris, W. W.: Rorschach estimates of personality attributes in the Michigan Assessment Project. *Psychological Monographs, 66:* Whole Number 335, 1–27, 1952.
25. Murray, H. A.: *Thematic Apperception Test Manual.* Harvard University Printing Office, Cambridge, Massachusetts.
26. Picque, L.: Du Delire Physique Postoperatoire. *Ann. Med. Psychologique, 8:* 91–105, 1898.
27. Potter, E. H.: An analysis of temporary situational factors upon Rorschach test results. Unpublished Ph.D. Thesis. Yale University, 1948.
28. Ruesch, J.: *Chronic Disease and Psychological Invalidism.* New York: American Society for Research in Psychosomatic Problems, 1946.
29. Sapirstein, M. R.: *Emotional Security.* New York: Crown Publishing Company, 1948.
30. Schneider, R. A., Gray, J. S., and Culmer, C. U.: Psychologic evaluation of surgical patients. *Wisconsin M. J., 49:* 285–290, 1950.
31. Sontag, L. W., Crandall, V., and Lacey, J. I.: *Dynamics of personality.* Resolution of infantile dependent need. *Am. J. Orthopsychiat., 22:* 534–541, 1952.
32. Sullivan, H. S.: *Conceptions of Modern Psychiatry.* Washington, D. C.: William A. White Foundation, 1940.
33. Sutherland, A. M., Orbach, C. E., Dyk, R. B., and Bard, M.: The psychological impact of cancer and cancer surgery. *Cancer, 5:* 857–872, 1952.
34. Wilcoxen, F.: *Some Rapid Approximate Statistical Procedures.* New York: American Cyanide Company, 1949.
35. Wittson, C. L., and Hunt, W. H.: The predictive value of brief psychiatric interviews. *Am. J. Psychiat., 107:* 582–585, 1951.

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PSYCHOSIS AND STUTTERING[1]

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Though the extensive European literature on stuttering does not seem to include any systematic study on stuttering among psychotics, there are scattered throughout it numerous isolated observations which have bearing upon our problem. The organicists among European investigators—represented by the School of Kussmaul-Gutzmann—were attracted especially by the not infrequent findings of stuttering in the brain damaged and the various neurological disorders (vascular, syphilitic, encephalitic, degenerative) affecting speech, an area which we would today, partly at least, comprise under the heading of "chronic brain syndrome" with or without psychosis. Others (1, 7, 8, 11, 21, 22, 27) stressing psychogenesis made notable contributions toward the phenomenology and psychopathology of stuttering. It was, however, not until quite recently (2) that the first systematic survey of a state hospital population concerning stuttering was undertaken in this country, and that the question of the distribution of stuttering among psychotics (2, 5, 31) and of the precipitation of a psychosis by the "removal" of stuttering was raised (31). Statistical studies on frequency and distribution of stuttering among psychotics and especially among the "functional" or major psychoses seem a distinct American contribution toward our knowledge on psychiatric aspects of stuttering.

The writer has thought it a challenging task to collect and survey these widely scattered fragmentary contributions to the problem "psychosis and stuttering"—an area common to psychiatry and speech pathology—and to submit them to a critical evaluation on the basis of: 1) his own extensive clinical observations on stuttering among psychotics; 2) a "total" approach to the problem of stuttering representing within the framework of psychopathology a synthesis of formerly isolated aspects; 3) our contemporary clinical-descriptive knowledge on the relationship between neurotic and psychotic phenomena and their mutual modifications and alterations to which this study may be considered as an additional contribution.

I. Frequency and Distribution of Stuttering among the Psychoses

1) Influenced by the spirit of time favoring an organic orientation, older European authors paid special attention to the not infrequent stuttering phenomena in conditions which we would today classify under the heading of "chronic brain syndrome" with or without psychosis. Bastian already, as quoted by Stockert (39), noticed that some cases of aphasia may start with stuttering. Stuttering as an initial or residual symptom of aphasia was described by Kauders, Dufour, Montier, Dejerine and others as quoted by Gutzmann (19). Kussmaul (23) coined the name "aphatic stuttering" which was later reintroduced by A. Pick and again by Gutzmann who even spoke of stuttering as a "focal symptom" of brain lesions and distinguished between "aphatic" and "dysarthric" stuttering. The latter quotes findings of iterative, stutter-like phenomena in cases of cortical and subcortical brain lesions by numerous authors (Cornil, A. Pick, Kalmus, Felix Kauders, Montier, Dejerine, Abadie, etc.). In all these instances stuttering accompanied and complicated primary aphasic or dysarthric disturbances. Gutzmann (19) also mentions one of the rare instances in the older literature, where a relationship between stuttering and the functional psychoses has been touched upon, by quoting Bruno Langes' dissertation on the speech of hebephrenics (Berlin, 1910) where stutte like reiterations without visible effort were described. A similar hint may be found in his passing remark that Heller's Dementia Infantilis which by some is considered as a rapid "schizophrenic" deterioration in early infancy may start "with some

[1] Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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kind of stuttering". Even Stockert (39), a pupil of Froeschels, who himself contributed notably toward our knowledge on the psychogenesis and socio-psychological factors of stuttering, in his monograph on the dissolution of speech in the psychoses does not mention a single case of stuttering among schizophrenics though he devotes special attention to stuttering—again of an iterative or clonic nature—among some general paretics, aphatics, post-encephalitics, etc. Stockert found this stuttering to be directly proportionate to the individual's level of awareness of the incongruency between speech drive and speech impairment and to disappear with increasing dementia. In cases of general paresis, effective malaria therapy, by restoring this awareness, led to a recurrence of stuttering. Luchsinger and Brunner (24) quote Féré who described stuttering occurring sometimes prior or following an epileptic seizure or even as an epileptic equivalent (?), which seems to contradict Stockert's (39) observation of stuttering disappearing during an epileptic twilight state. It may be assumed that the decisive factor is the degree of cloudiness of sensorium: slight degrees of clouding may favor stuttering whereas deeper disturbances of consciousness are prone to eliminate it. Luchsinger (25) described recently two cases of "organic" stuttering in individuals with objective signs of brain damage. The designation "organic" should, however, not deter us from realizing, as stressed already by Stockert (39), that stuttering in the organically brain damaged represents a simple psychogenic hypercompensatory reaction, whereby the psychological factor of awareness of the conflict between speech drive and speech accomplishment is of crucial importance.

2) Systematic observations of a statistical nature were made on stuttering among mentally defective children where it was found to be as high as 14% (Knopf) with a sex ratio between boys and girls of 2 to 1. Piper, however, found only 7% stutterers among mentally defectives (quoted by Gutzmann (18)). Gens (14), in this country, pointed to the conspicuous frequency of stuttering among mongoloids. We may assume—on theoretical grounds—that stuttering probably will be found more frequently among the versatile and hyperkinetic forms of mental deficiency than among the torpid and hypokinetic ones and more among those with a higher than with a lower I.Q.

3) A paper by Barbara (2) contains probably the first systematic study on stuttering among a state hospital population. Among 7,000 patients of the Central Islip State Hospital (Long Island, New York) stuttering was found in only 20 cases, which means 1 stutterer among 350 patients or 0.28% as contrasted to 1% of stutterers assumed to exist among the general population. Barbara (2) rightly assumed that it is difficult to arrive at any certainty concerning frequency from such a survey since only "those patients who exhibited definite symptoms of stuttering were selected", excluding those who were mute, disturbed or resistive and those whose stuttering was masked by some "allied disorder". In table 1 is given the distribution of stuttering among the various categories of a state hospital population cited by Barbara in his study (2). It seems that two of these patients (psychasthenia and pathological intoxication) were actually not psychotic.

TABLE 1.—Distribution of Stuttering among 7,000 State Hospital Patients Found by Barbara (1946)

Dementia praecox:	
Paranoid	6
Hebephrenic	4
Catatonic	1
Psychosis due to convulsive disorders	3
Manic depressive psychosis	2
Psychoneurosis:	
Psychasthenia	1
Alcoholic psychoses:	
Pathological intoxication	1
Psychosis due to mental deficiency	1
Psychosis with epidemic encephalitis	1
Total	20

Barbara concludes from his findings that the majority of stuttering psychotics are of schizoid make-up, and at the same time he postulates that the personalities of psychotic and neurotic stutterers differ only in degree. His findings, however, would suggest a considerable prevalence of stuttering among the psychoses with convulsive disorders which becomes especially obvious if one considers not the absolute but the relative frequency of schizophrenic and epileptic stutterers. According to the Annual Report of the Department of Mental Hygiene of the State of New York there were in 1946

only 126 epileptics at the Central Islip State Hospital compared with 5,041 schizophrenics. Among those 5,041 schizophrenics were 11 stutterers (0.22%); whereas among 126 epileptics were found 3 stutterers (2.4%). This would suggest that the frequency of stuttering among psychoses with convulsive disorder was approximately 10 times higher than among schizophrenics.

Pitrelli (31) from the same hospital was unable to find among 300 psychotic females a single case of stuttering, but from their history he discovered that 3 of them were former stutterers. He concluded from this that stuttering among mental patients may be as frequent as among the general population (1%). He omitted to consider, however, that the frequency of stuttering among females is at least 4 or 5 times smaller than among males, a fact which would invalidate his conclusions and raise the frequency above that found in the general population.

During a 4-year period of observation the writer was able to find 17 cases of stuttering among the population of a "mixed" service of approximately 450 patients at the Rochester State Hospital, Rochester, New York, with wards for acutely disturbed, quiet and improved, semidisturbed, senile and arteriosclerotic and regressed and infirm patients and a turnover of between 100 to 120 patients a year. The number of stutterers simultaneously present at this service fluctuated within a wide range according to the constantly changing population. The distribution of the 17 cases of stuttering observed is given in table 2. The similarity with Barbara's (2) findings is obvious, with an almost identical ratio of epileptics (17 to 3) but also with a conspicuous number (4) of individuals falling into the dubious category of "psychopathy". The great fluctuation in the number of stutterers which were seen simultaneously at the service makes the writer dubious about any *ad hoc* survey based upon a relatively small number of patients.

Between January, 1954, and February, 1955, the writer made notations on speech disorders with special considerations to stuttering and tachylalia at a VA Mental Hygiene Clinic (VA Regional Office, Milwaukee, Wisconsin). The veterans diagnosed as schizophrenic reaction were all ambulatory, in a satisfactory or partial state of remission, and partly employed. Among 149 so diagnosed veterans, there were 5 cases of unquestionable stuttering (3.2%), a finding which would cast further doubts upon the claimed rarity of stuttering among psychotics. Actually no significant difference in the frequency of stuttering among a group of "psychoneurotics" and psychotics could be found. In table 3 these two categories are compared with each other. (Atypical and pseudo-stuttering will be discussed in the next chapter.)

Bolin (4) found 4 stutterers among 300 mental patients at a state hospital, concluding from this that the incidence of "conspicuous stuttering" among the functionally psychotic is probably higher than quoted for the general population.

TABLE 2.—DISTRIBUTION OF STUTTERING AT A "MIXED SERVICE" OF 450 PATIENTS AT A STATE HOSPITAL DURING A 4-YEAR PERIOD (H. FREUND, 1950 TO 1953)

Dementia praecox:	
Paranoid	4
Hebephrenic	1
Catatonic	1
Undifferentiated	1
Psychosis due to convulsive disorders	2
Manic depressive psychosis	1
Psychosis with psychopathic personality:	
With convulsions	1
Without convulsions	3
Psychosis with mental deficiency	1
Psychosis with cerebral arteriosclerosis plus aphasia	1
General paresis	1
Total	17

TABLE 3.—COMPARISON OF FREQUENCY OF STUTTERING AMONG 2 GROUPS OF VETERANS

Psychiatric Category	Total No. Cases	Clutter-Stuttering	Stuttering	Total and %	Atypical Stuttering	Pseudo-Stuttering	Cumulative Total %
Psychoneurosis	225	2	7	9 (4%)	8	1	18 (8%)
Schizophrenic reaction	149	1	4	5 (3.2%)	2	5	12 (8%)

4) A survey conducted by Wise (45) at the State Institution for Epileptics at Craigh Colony, Sonyea, New York, revealed 38 cases of stutterers among 2,348 epileptics (1.6%). The mean I.Q. of this group of stuttering deteriorated epileptics was in Dr. Wise's opinion in the neighborhood of 50 or 60. A critical evaluation of this finding, however, must lead to the conclusion that the percentage of stuttering among "deteriorated" epileptics is probably higher since only conspicuous cases were selected without a systematic study of the speech of all the inmates of the institution.

This assumption seems to have been confirmed by the findings of Gens (13) at the Caro State Hospital for Epileptics, Caro, Michigan (1950). In a search after a reliable diagnostic sign for epilepsy, Gens made a detailed study of the speech deviations. In 297 cases the speech was normal. He noticed that 205 had "no speech". Plateau speech (monotony) which is usually considered as pathognomonic for epilspsy (see Luchsinger and Brunner (24)) was found to be even less frequent than stuttering. There were no less than 47 stutterers found, and only 41 persons had plateau speech. The relatively high percentage of 3.7% stutterers among these institutionalized epileptics contrasts conspicuously with the 0.22% of stutterers among institutionalized schizophrenics found by Barbara. It is, however, essentially not different from the percentage of stutterers among ambulatory schizophrenics, representing milder forms of schizophrenic reactions, which were observed by us among veterans (3.2%).

Bolin (5), in a continuation of the search for a sign diagnostic for epilepsy (1953), compared left handedness and stuttering in groups of 76 epileptics, oligophrenics, hebephrenics and paranoid schizophrenics. Increased incidence of migraine, left handedness and stuttering was found in families of epileptics previously by Steurer, Heilig, etc. (as quoted by Luchsinger (24)). Bolin's findings of as high a frequency as 13% of "stuttering" in the group epileptics and hebephrenics can be used here only with some modifications since, what he originally called "stuttering", was actually only a "dysrhythmia" of speech and not genuine stuttering and included probably also what we ourselves have called "pseudo-stuttering", a concept which will be more extensively discussed in the next chapter.

Discussion and evaluation of findings

1) Up till now the problem of frequency and distribution of stuttering among the various psychoses has not yet been solved satisfactorily, and the few fragmentary attempts in this direction seem inconclusive. Even the most fundamental question whether there is a significant difference in the frequency between stuttering among the functionally psychotic and the general population has not yet been satisfactorily solved. Without venturing to arrive at fargoing conclusions from the observations of relatively small groups, our own observations would at least throw some doubt upon the alleged great rarity of stuttering among the functionally psychotic.

2) There seems to be a considerable difference in the frequency of stuttering between institutionalized schizophrenics and epileptics. We may assume that the growing discrepancy between organic deterioration of thought processes and speech faculty on one side and the generalized increased "explosive" excitability and tendency to perseveration (Stauder) on the other side in these epileptics is a factor favoring stuttering, whereas a tendency toward early withdrawal, diminished drive, emotional flattening and disinterest in the use of speech for communicative purposes in certain categories of schizophrenics has the opposite effect. Of great interest is also the apparent greater frequency of stuttering among ambulatory, mild or arrested cases of schizophrenia if compared with the more severe and regressed institutionalized schizophrenics.

3) The understanding of such quantitative differences (increased frequency of stuttering among institutionalized epileptics, mentally defective clutterers, ambulatory schizophrenics, neurological speech disorders, etc.) requires a wider frame of reference than that given by any exclusive school of "psychodynamics". It requires a "total approach" representing a synthesis of psychogenetic, psychosocial, phenomenological, clinical and constitutional aspects, whereby the etiological importance of possibly existing deficiencies of the function of speech itself is not being overlooked.*

4) The question may be raised whether a comparison between the differences of stuttering among the various categories of neurotics, the personality disorders, epileptics, functionally psychotic, etc., may not constitute a new lead in the endless search for the characteristics of the personality of stutterers which is today being pursued by the application of innumerable tests and projective techniques. A critical evaluation of these results would speak for a great variety of personality types being susceptible to "stuttering" as was recently also pointed out by Shames and Matthews (36) on the basis of extensive psychological studies. This is in accordance with our clinical observation that stuttering can be found in the most divergent categories of psychotics, neurotics, psychopaths, etc., with one notable exception, this exception being the manic-depressive reaction type. Not as yet has a single case of typical or "pure" manic-depression with stuttering been described. Two cases mentioned by Barbara and one observed by us exhibited definite schizoid admixtures.

II. Observations on Stuttering in Schizophrenics

Sources and methods of observation

Our observations on qualitative characteristics of stuttering among this category of psychotics are based upon a group of 27 schizophrenics with stuttering or stutter-like speech. This group was compounded from various sources over a period of years: One case ("atypical" stuttering) was observed among private patients (Yugoslavia, 1937); seven cases during a 4-year period of observation at a state hospital (1950–1953) of which there were one "atypical" and one pseudostutterer; 12 cases during a 14-month observation at a VA Mental Hygiene Clinic (1954–1955) (table 3); and 7 cases were reported in personal communications by Bolin from his observations at several state hospitals. Our method consisted of making regular notation on stuttering, stutter-like speech, tachylalia, monotony or other outstanding speech characteristics during psychiatric interviews. The attention was especially centered upon: 1) the characteristic mode of stuttering and 2) the degree of awareness and the manner in which the individual experienced his stuttering. We intend to give illustrative case material in detail in another presentation. Here we want to limit ourselves to a general outline of what we consider as characteristic features of stuttering among schizophrenics on the basis of our observations.

Outline and Discussion of Findings

1) We consider *persistency* of stuttering in schizophrenics as an outstanding and up to now practically overlooked phenomenon. In one case observed by us, stuttering in a concealed form withstood such procedures as repeated ECT, insulin coma therapy and an extensive bi-frontal lobotomy and has persisted in spite of severe regression and many years of mental illness. This *concealment* (under the mask of mutism, withdrawal, stupor, mannerisms and non-use of speech for communicative purposes, pointed at already by Barbara) seems to present another characteristic feature of stuttering in regressed schizophrenics. When "forced" to reply instead of mumbling in response to auditory hallucinations, the above-mentioned, regressed patient still exhibited stuttering. Under emotional outbursts of a hostile character or during a flare-up of the psychosis, "concealed" stuttering may again become manifest and demonstrate its persistency. Several such cases have been observed by me, and Bolin (6) has described three cases where, during such acute episodes, hitherto unnoticed stuttering became manifest for the first time. It seems that even a very low degree of awareness of the social implications seems to suffice to perpetuate such a neurotic symptom as long as accompanying affects and attitudes (aggression, hostility, coupled with fear, inner vacillation, ambivalence, etc.) continue to exist.

In general the less marked this "regression", the more open and manifest stuttering remains. This is seen in the apparent prevalence of stuttering among schizophrenics in a good or partial state of remission (3.2% among schizophrenics seen at the VA Mental Hygiene Clinic) if compared with findings among institutionalized state hospital patients (0.22% Barbara; 1.4% Bolin).

2) *Stutter-like speech* (*"pseudostuttering"*) *and "atypical"* (*hysterical*) stutter phenomena

seem to be fairly frequent in schizophrenics and to overshadow in frequency genuine stuttering (table 3). The phenomena in question can be understood only within the framework of the fundamental investigations by Froeschels (12) about what the criteria of common or genuine stuttering are. He defined the typical stutter tonus as being characterized by a positive relationship between the duration, effort and—I would add—affect, which means that the longer the duration of a tonic effort the stronger is the force invested and the affect released.

On the basis of this criteria, Froeschels (12) was able to distinguish between stuttering acquired by imitation and "typical", developmental or genuine stuttering merely by the minute observations of symptoms. In recently acquired imitation or induced stuttering (Weiss and Barczinski (43))—similarly as in recently acquired hysterical and traumatic stuttering—the positive relation between duration, effort and affect is lacking in spite of the individual's full awareness of a speech hurdle. We see here tonic interruptions and stoppages but without the spasmodic effort to overcome the hindrance with enormous force which is so characteristic of the developmental stuttering. Here we may speak of "atypical" stuttering although, as Bleuler (3) put it, there is nothing atypical in nature and what we call typical is only a matter of arbitrary classification. This "atypical" stuttering in our opinion is of a conversion hysterical nature. In "pseudostuttering" or stutter-like speech even the awareness of a speech obstacle or difficulty in enunciation is lacking. Several such cases in schizophrenics in remission were observed who definitely impressed as "stutterers" but who obstinately denied that speaking to them is difficult. Instead, they explained the constant hesitation, reiterations, stoppages and minute tonus-like efforts as being purely the result of forgetfulness, undecisiveness, poor word memory, inner conflicts, etc. When combined with hastiness, pseudostuttering becomes indistinguishable from cluttering. Bolin (5) found "dysrhythmia" in schizophrenics in a very high percentage of cases (13%). Pseudostuttering may be considered as a transitional stage between simple dysrhythmia and stuttering.

3) Thinking and speech disturbances in the beginning of a schizophrenic development may render the individual speech conscious. One case was observed where the onset of stuttering coincided with the onset of the psychoses. This stuttering, however, was of an atypical, conversion-hysterical type. Several cases of incipient schizophrenic reactions were observed where the patients complained about not being well-understood by others, of being talked about, and teased on account of their speech peculiarities and who therefore started to avoid talking to other people. Schizophrenic thinking and speech peculiarities (Kraepelin's "schizophasia") (35) may intensify an already existing deficiency in the expressive faculties. Two cases with a history of marked retardation in speech development were seen who—following a schziophrenic episode—showed a further reduction in their communicative faculties with an overlay of stutter-like symptoms (pseudostuttering).

4) Since in some schizophrenics the history reveals that stuttering has existed in childhood and that they apparently lost their stuttering prior to the outbreak of their psychosis (Pitrelli), one must conclude that spontaneous recovery from stuttering does not necessarily imply a favorable prognosis for the personality as a whole. However, our observation on the persistency of stuttering even in regressed schizophrenics would completely contradict the claim that stuttering itself can serve as a defense against a psychosis and that the "removal" of stuttering—without the necessary psychotherapy—may lead to an outbreak of a psychosis (31). In our opinion the idea that a person can be "deprived" of his stutter (41) is quite unrealistic since, like in any other field of psychotherapy: a) any improvement during the treatment of stuttering is the result of a joint collaborative effort and b) unfortunately, nothing is more certain than a relapse or recurrence of stuttering in a person who is allegedly "cured" but continues to feel insecure and fearful of approaching people. We may, however, consider the possibility that occasionally a stutterer desiring therapy may be in the process of developing a psychosis or very close to it as was obviously the case in two cases reported by Meyer (28).

5) The impression was gained that stuttering for psychotics, especially those with "regression" or emotional flattening, is usually of much smaller importance—playing as it were

only an insignificant role—compared with the typical severe (neurotic) stutterer for whom stuttering becomes "the" central life issue. This diminished suffering in relation to stuttering was especially illustrated by following self-description of a schizophrenic in good remission: "After I became mentally ill and spent a year in a mental institution, I realized that there are many worse things in the world than stuttering. I think I lost a part of my former pride and vanity and now though I still stutter, I don't care so much about it." This change of feelings and attitudes may result in an amelioration of the severity of stuttering though apparently not in its complete cessation.

A similar impression was gained from the observation in other generally disturbed but non-psychotic patients (severe anxiety neurotics, conversion hysterics "psychopaths", etc.). In all these individuals stuttering played a rather inconspicuous role in their symptom complex, and not one among them complained spontaneously about his speech.

III. Parallel Phenomena in Stuttering and the Psychoses

A search into the inner experiences of the stutterer suggests certain features kindred, related, or analogous to features observed in psychotic resolutions.

1) Through the study of *internal speech* an interesting relationship has become apparent between the vivid anticipatory experiences of some stutterers and the hypothetical mechanism involved in auditory hallucinations of psychotics. The anticipation of impending stuttering has been previously described by Hoepfner (22) and Appelt (1), on the basis of self-observation, as being prone to approach a hallucinatory clearness and intensity. As a result of similar introspective observations, Freund (8) advanced the concept of "internal stuttering" via internal speech, stressing its ideo-motor aspects in contrast to the purely ideational explanation of Hoepfner and Appelt. He also observed the vivid anticipation experience of difficulty but in addition noticed also minute ideo-motor or Einstell movements of the speech organs, accompanying the stutterer's attempt to overcome the hindrance inwardly, which by a process of self-induction ("negative feedback") intensifies his feeling of difficulty. The same phenomenon was later called "preparatory set" by Von Riper (42). "Rehearsal movements" and increased muscle tonus of the speech organs, etc., during the expectancy period prior to the speech attempt were demonstrated pneumographically, myographically and plethysmographically by Von Riper, Strother, Fletcher and Robbins (as reported by Von Riper (42)). Gould (16, 17) has, in several studies on auditory hallucinations, pointed to increased muscle tension states in the vocal cords demonstrable through electromyography and to "subvocal speech" which could be made audible by means of microphones and electrical amplifiers during auditory hallucinations. Gould rejects the exclusively ideational nature of auditory hallucinations but instead thinks that we are dealing here with "automatic speech" and its motor manifestations in the vocal cords which the individual experiences as ego alien. Others (Roberts, Greenblatt, and Solomon (32)) were unable to confirm that subvocal speech or Einstell movement of the larynx is a necessary element in auditory hallucinations. Similar objections may be raised against the theory that Einstell movements are of essential importance in the anticipatory experience of impending stuttering. In both instances these internally perceived, involuntary, minute movements of the speech organs are frequently associated with but probably not the primary cause of the phenomena in question.

2) Severe crippling personality changes of a quasipsychotic nature in some chronic and "severe" stutterers were described by numerous authors, e.g., Merkel (27), Denhardt (7), Hoepfner (21), Froeschels (11), Glauber (15), etc. Withdrawal, depression, moodiness, asocial and even anti-social tendencies and "distortion of logic and ethics" were stressed by these authors which seem contradictory to the concept of "secondary gain" stressed especially by individual psychologists like Appelt (1). No detailed case histories about individual stutterers with such a grave outcome, however, were ever presented. Taken as granted that their observations were correct, the question arises as to the underlying personality type predisposing to such a prognostically grave course. Hoepfner (21) has tried to explain the severity of secondary personality changes, which Glauber (15) rightly defines as "character neurosis", primarily by "constitutional"

factors. That the parallelism between constitution, personality disturbance and stuttering is not absolute is shown by the occurrence of slight degrees of stuttering or even of spontaneous recoveries in individuals who later developed a psychosis and of an insignificant degree of stuttering in persons with severe anxiety neurotic or severe personality disturbances. The apparently complete different significance which stuttering assumes for different individuals with its prognostic implications represents a problem which has not as yet been clearly formulated and which may form an interesting field for future research.

3) Distortion and misinterpretation of reality, projections, narrowing of consciousness, etc. are phenomena considered as pathognomic of a psychotic state, but they are also commonly observed in states of panic and also seem to be experienced as transient phenomena by sensitive stutterers during an act of "severe" stuttering in a socially unbearable setting. ("Severe" is meant here to connote the intensity of the emotions and of subjective suffering and not merely the severity of the physical effort accompanying stuttering.) The panic character underlying the emotional upheaval during such an act of stuttering was underlined by Meyer Solomon (37) and the writer (9). We have pointed out previously (9) that the accompanying affect, "steadily reinforced through self-induction, may render the stutterer unable to judge the situation objectively. It may appear highly dangerous in a social sense. The feeling of being helplessly exposed to the arbitrary power of the listener may be so strong that paranoid misinterpretations of the situation and of the attitude of others may occur. As in any traumatic or panic situation of high affective discharge the clearness of logical thinking, memory and judgment may become momentarily impaired." A closer analysis and experimental psychological study on the manner how individual stutterers experience themselves, their impediment and their surroundings during acts of "severe" stuttering would be of value not only in disclosing important individual dynamics (for instance hidden paranoid trends) but also in contributing toward our knowledge on "cathatymic" psychotic-like states in the neuroses and to the psychopathology of panic states.

4) Many stutterers and schizophrenics complain similarly about their becoming very easily confused when having to talk publicly or with strangers. A similar shyness with lack of ease in approaching people and in communicating with them was described as a pronounced characteristic of the so-called "social neurosis" by Schilder (34) and of the "social anxiety neurosis" by Meyerson (29). The close relationship between these "neuroses" and the paranoid schizophrenic reaction type has been pointed out by Meyerson. While the feeling of confusion and thought dissociation in prepsychotic states usually results in increasing avoidance of social contacts, according to the strong tendency towards withdrawal, there have been cases of stuttering seen starting or being aggravated in this phase. We have pointed out (10) that this lower threshold for dissociation of inner speech functions under emotional stress may constitute one of the "functional inferiorities" upon which—in certain groups of stutterers—the disturbance may develop as a kind of faulty overcompensation in the Adlerian sense.

5) *Illusionary distortions of self-estimation* were stressed especially by adherence of individual psychological and neo-analytic (Horney) schools, stuttering being considered by some stutterers as the only cause for all their inadequacy and their unsuccessful career, maintaining in this way the illusion of nonexisting virtues, powers and capabilities. There are also negative illusional distortions in the direction of an extremely low self-esteem and the overestimation of the values of others in some stutterers. Between such illusional distortions and the frank delusions of psychotics, there are certain though remote analogies.

It may be said that such analogies with phenomena in psychotics, as enumerated here, and to which many others could be added, cannot in any way be considered as specific for stuttering but can be found on closer scrutiny in all other neurotic disturbances. However, more severe distortions of interpersonal relationships, self-estimation and even intellectual functioning may be expected in a neurotic disturbance of speech existing since early childhood. We may consider as possibly more "specific" analogies: a) the apparent diminished threshold for confusion and thought

dissociation under "social" stress in certain stutterers and schizophrenics and b) the similar role which internal speech plays in the mechanism of anticipation of stuttering as well as in auditory hallucination.

6) An interesting parallelism to stuttering in the organic psychoses—where stuttering develops as a simple psychogenic overlay upon organic speech defects of an aphasic or dysarthric nature—was found through the study of the relationship between stuttering and cluttering (Weiss (44); Freund (10)). It was found that there is a type of so-called clutterers whose speech hastiness is part of an organic syndrome which is characterized by constitutional defects in speech endowment and which Weiss (44) has described under the heading of "central speech imbalance". In such instances of chronic communicative insufficiency stuttering may develop as a psychogenic, hypercompensatory mechanism similarly as it was previously described in the neurologic speech disturbances, the brain damaged, aphatics and "deteriorated" epileptics.

IV. Psychiatric Implications

The connections and interrelationships between neuroses, psychosomatic disorders and psychoses from a clinical and descriptive point of view have been extensively studied. Their study represents one of the most fascinating chapters of clinical psychopathology. Similar problems seem to have been encountered in all these investigations, and the analogies to our own studies are many. These similarities are especially obvious when studies on the frequency of stuttering among psychotics are compared with those on the incidence of psychosomatic disorders among the mentally ill, as recently summarized by Ross (33). There too the difficulty in detecting the disorders in psychotics presented itself as a serious obstacle. As in the case of stuttering the incidence of psychosomatic disorders among psychotics, according to various authors, varies within a very wide range, and here too, on ideological grounds, a reciprocal relationship with the psychoses was claimed but not generally confirmed. Macalpine (26) underlined the important fact that psychosomatic symptoms ("neurodermatitis") not infrequently mask and conceal an underlying psychotic process reminding us of pre-psychotic or mild psychotic states where stuttering may be the leading symptom. Reports on the outbreak of a psychosis in long standing psychosomatic disorders following or during therapy by Jeliffe and Joseph (see Ross (33)) are paralleled by similar sporadic observations in stutterers.

Hoch and Polantin (20) have shown that neurotic symptoms not only may completely mask an underlying schizophrenic development ("pseudoneurotic schizophrenia"), but that in such cases these symptoms as well as the course and character of the psychosis become "atypical". Our observation on the not infrequent qualitative and quantitative changes of stuttering in the psychoses bears some resemblance with their findings. Stengel (38) found that a pre-existent obsessive compulsive neurosis renders a schizophrenic psychosis milder but a depression more severe, and Noble (30) stressed that the combination of conversion hysteria and schizophrenic reaction enhances the chances of successful psychotherapy. No such direct and predictable relationship could be established between stuttering and the severity of a psychosis, and all degrees of regression were seen in stuttering psychotics. The conditions here are necessarily more complex since various combinations of psychopathological mechanisms and a great variety of personality types may be underlying the symptom of "stuttering" (9)(36)(40).

It is of special interest, since stuttering in its most important forms deserves to be classified under the heading of expectancy neurosis, that Bleuler (3, 4) already has stressed the frequency of "expectation neuroses" (Isserlin, Kraepelin) in schizophrenics, pointing out that they may even dominate the picture and mask an underlying schizophrenic reaction. He stressed the interesting point that in such an instance one will rarely find an isolated expectation neurotic symptom but usually several combined. To this we can add that, as in stuttering, the quality of the expectancy neurotic symptom also becomes changed. "Stuttering" which in its fully developed forms is one of the classical expectation neurotic disturbances may appear, as shown in this study, either in an atypical (conversion hysterical) or "pseudo" form or lose its significance in the inner experiences of the sufferer, becoming an "incidental" symptom. It may become completely overshadowed and pushed

into the background by gross psychotic manifestations or masked by stupor, mutism and withdrawal only to become manifest again when aggression and hostility reappear during an acute flare-up of the psychosis. Theoretically one should assume that the deepening regression in some schizophrenics should tend toward a complete elimination in analogy to what is said to occur in the progressive dementias of the organic psychosis. Actually ours and Bolin's observations would tend toward the bèlief that there is a considerable tendency of stuttering to persist even under such circumstances though often in a milder and more concealed form.

Of clinical importance may be the fact that in rare instances in the pre-psychotic state or in the "pseudoneurotic type" of a schizophrenic reaction, stuttering may be the leading symptom and lead to erroneous attempts of "speech therapy" as illustrated by case histories of stutterers becoming manifestly psychotic during therapy. Another point of clinical interest may be the fact that in some cases the initial phases of a schizophrenic development or a residual state following a schizophrenic episode is characterized by marked speaking and thinking disturbances rendering the individual "speech conscious" and leading, by the way of a hypercompensatory mechanism, to considerable reiterations, hastiness and even to occasional tonic efforts—a kind of "pseudostuttering" which is difficult to distinguish from genuine stuttering except for the fact that the patient has no awareness of speech blocks. The schizophrenic basis of this disorder may remain unrecognized and the "stutterer" subjected to futile attempts at "speech correction".

V. Summary and Conclusions

1. European and American contributions to the problem of the relationship between psychosis and stuttering were reviewed, evaluated and compared with the writer's own observations on stuttering in psychotics.

2. On the basis of the few studies conducted so far—mostly on relatively small groups of psychotics—no definite statements on frequency and distribution of stuttering in certain groups of psychotics can be made in comparison with the general population. The impression is that there is a definite increase of stuttering among some groups of organic psychoses (e.g., institutionalized epileptics) and among mentally defective children, and that even among regressed schizophrenics, where it may be difficult to detect, stuttering is not as infrequent as has been claimed. In a group of 149 "ambulatory" schizophrenics, three times as many stutterers were found than is assumed to exist among the general population. No stuttering has up till now been described in a typical manic-depressive psychosis. The few cases mentioned under this heading all exhibit definite schizoid admixtures.

3. Studies on frequency and distribution of stuttering among the various categories of functional and organic mental illnesses and other groups of "deviates" (mental defects, personality disorders, etc.)—if critically analyzed and evaluated—may represent a new lead in the search for important personality and etiologic factors in stuttering. The results can be properly understood, however, only from a synthetic or total point of view which, in addition to psychodynamics and sociopsychological factors, stresses also psychophysiology, constitutional factors and possible deficiencies of the function of speech itself.

4. The relative frequency of "atypical" or conversion-hysterical and of stutter-like speech or pseudostuttering in schizophrenics was underlined, and their characteristic features and differential diagnosis from "genuine" stuttering (Froeschels) were given.

5. A considerable persistency of stuttering in spite of regression and long duration of mental illness was found. This would speak against the reciprocal relationship between psychosis and stuttering claimed by some authors. Detection may be difficult because of "concealment" by gross psychotic symptoms. Without completely disappearing stuttering may lose in importance and become an "incidental" symptom. Acute flare-ups of the psychosis may again reactivate it.

6. The fact that a certain, though relatively small, group of stutterers are potential, active or residual schizophrenics has been definitely established. This again shows the necessity of psychiatric knowledge and experience in persons treating adult stutterers.

7. Some analogies between stuttering and

the psychoses were described. They cannot be considered as specific since transitory perceptual distortions and constrictions of intellectual functioning of an identical nature are encountered in all emotionally highly charged conditions especially in phobias and panic states. However, more severe and more permanent distortion of interpersonal relationships and of self-estimation can be expected in a neurotic disturbance of speech existing since early childhood. More "specific" analogies concern a) the important role of internal speech in the mechanism of anticipation of stuttering and of auditory hallucinations, b) the increased "social anxiety", and c) the possible diminished threshold for confusion and thought dissociation under "social" stress.

8. A comparison with contemporary psychosomatic research and with studies on the relationship between the neuroses and the psychoses, on a clinical descriptive basis, reveals: a) that similar problems, difficulties and uncertainties have previously been encountered in the wider field of the study of the relationship of psychosis and psychosomatic disorder; b) that the described qualitative peculiarities of stuttering in psychotics are, in some way, analogous to the general modification of other psychoneurotic symptoms in the psychoses as, e.g., described by Hoch and Polantin for anxiety and by Stengel for obsessions and compulsions. The conditions here are more complex since various psychopathological and neurotic mechanisms may underlie the symptoms of "stuttering".

BIBLIOGRAPHY

1. Appelt, A.: Sprachstoerungen. In Wexberg's *Handbuch d. Individualpsychologie*. Muenchen: Bergmann, 1926.
2. Barbara, D. A.: A psychosomatic approach to the problem of stuttering in psychotics. *Am. J. Psychiat., 103:* 188, 1946.
3. Bleuler, E.: *Dementia Praecox of the Group of Schizophrenias*. Translated by J. Zinkin. New York: International University Press, 1950.
4. Bleuler, E.: *Lehrbuch der Psychiatrie*. Berlin: Julius Springer, 1916.
5. Bolin, B. J.: Left-handedness and stuttering as sign diagnostic for epileptics. *J. Ment. Sc., 99:* 483, 1953.
6. Bolin, J.: Personal communication, March 4, and 5, 1955.
7. Denhardt, R.: *Das Stottern. Eine Psychoses*. Leipzig. Ernst Keils Nachfolger, 1890.
8. Freund, H.: Inneres Stottern und Einstellbewegung. *Zeitschr. f. ges. Neurol. u. Psychiat., 138:* 104, 1932.
9. Freund, H.: Psychopathological aspect of stuttering. *Am. J. Psychotherapy, 7:* 689–705, 1953.
10. Freund, H.: Studies in the interrelationship between stuttering and cluttering. *Folia Phoniatrica, 4:* 146, 1952.
11. Froeschels, E.: *Lehrbuch d. Sprachheilkunde*, 3rd ed. Leipzig and Wien: Franz Beuticke, 1931.
12. Froeschels, E.: Imitation stuttering. *Folia Phoniatrica, 6:* 178–185, 1954.
13. Gens, G. W.: Correlation of neurol. findings, psychol. analyses and speech disorders among institutionalized epileptics. *The Training School Bulletin, 47:* 3–18, 1950.
14. Gens, G. W.: The speech pathologist looks at the mentally deficient child. *The Training Bull., 48:* 19–22, 1952.
15. Glauber, J. P.: Orientation in the stuttering problem. *"Eye, Ear, Nose & Throat Monthly, 16:* 223, 1937.
16. Gould, L. N.: Verbal hallucinations and activity of vocal musculature. *Am. J. Psychiat., 105:* 367, 1948.
17. Gould, L. N.: Verbal hallucinations as automatic speech. *Am. J. Psychiat., 107:* 110, 1950.
18. Gutzmann, H.: *Die soziale Bedeuting der Sprachsoerungen*. Jena: Gustav Fischer, 1904.
19. Gutzmann, H.: *Sprachheilkunde*, 3rd. ed. Edited by H. Zumsteg. Berlin: H. Kornfeld, 1924.
20. Hoch, P., and Polantin, P.: Pseudoneurotic forms of schizophrenia. *Psychiat. Quart., 23:* 248–276, 1949.
21. Hoepfner, T.: Stottern als Assoziative Aphasie. *Zeitschr. f. Pathopsychologie, 22:* 544, 1912.
22. Hoepfner, T.: "Zur Klinik und Systematik d Associativen Aphasie," *Zeitschr. f. ges. Neurol. u. Psychiat., 79:* i, 1922.
23. Kussmaul, A.: *Stoerungen der Sprache*, 4th ed. Edited with comments by H. Gutzmann. Leipzig: F. C. Vogel, 1910.
24. Luchsinger, R., and Brunner, R.: Exp. Phon. Untersuchung d. Sprache und Sprachstoerungen d. Epileptiker. *Folia Phoniatrica, 2:* 79–98, 1950.
25. Luchsinger, R.: Gibts es organisch bedingte Stotterfaelle? *Arch. Ohren-Nasen- u. Kehlkopfheilk. u. Z. Hals- Nasen- u. Ohrenheilk. 165:* 612–618, 1954.
26. Macalpine, I.: Present status of psychosomatic medicine. *Am. J. Psychotherapy, 8:* 454–465, 1954.
27. Merkel, C. L.: Stottern. In *Encyklopadie d. ges. Medizin*, hrsg. Leipzig: v. C. Ch. Schmidt, 1842.
28. Meyer, B. C.: Psychosomatic aspect of stuttering. *J. Nerv. & Ment. Dis.*, 101: 2, 1945.
29. Meyerson, A.: The social anxiety neurosis. *Am. J. Psychiat., 101:* 149, 1944.
30. Noble, D.: Hysterical manifestations in schizophrenic illness. *Psychiatry, 14:* 153–160, 1951.
31. Pitrelli, F.: Psychosomatic and Rorschach aspect of stuttering. *Psychiat. Quart., 22:* 175, 1948.
32. Roberts, B. H., Greenblatt, M. and Solomon, G. C.: Movements of vocal cords during auditory hallucinations. *Am. J. Psychiat., 108:* 912, 1952.
33. Ross, D. W.: Psychosomatic disorders and psychoses. Chapter 22, pp. 397–418. In *Recent Developments in Psychosomatic Medicine*. Ed. by Wittkower & Cleghorn. Philadelphia, Montreal: J. B. Lippincott Co., 1954.
34. Schilder, P.: *Psychotherapy*. New York: W. W. Norton Company, Inc., 1951.
35. Schwab, H.: Die Schizophasien. *Arch. f. Psychiat. u. Nervenkrankh. Z. f. ges. Neurol. u. Psychiat., 182:* 335–399, 1949.

36. Shames, G. H. and Matthews, J.: Comparison of personality test scores of stutterers and non-stutterers. Lecture, 30th Annual Convention, St. Louis, Mo., Oct., 1954.
37. Solomon, M.: Stuttering and an emotional and personality disorder. *J. Speech Dis., 4:* 547–557, 1939.
38. Stengel, E.: A study on some clinical aspects of the relationship between obsessive neurosis and the psychotic reaction type., *J. Ment. Sc., 41:* 166–187, 1945.
39. Stockert, F. G. v.: *Ueber Umbau und Abbau der Sprache bei Geistesstoerung.* Berlin: S. Karger, 1929.
40. Šubert, M.: Zur Psychopathologie, Klinik und Therapie d. Stotterns. *Zentralbl. f. ges. Neurol. u. Psychiat., 52:* (2), 1929.
41. Travis, L. E.: The need for stuttering. *Speech J. Dis., 5:* 193–208, 1940.
42. Von Riper, C: The preparatory set in stuttering. *J. Speech Dis., 2:* 149–154, 1937.
43. Weiss, D., and Barczinski, K.: Zur Erkennung d. Nachahmungsstotterns. *Arch. f. Psych. & Nervenkrkheiten, 95:* 321–329, 1900.
44. Weiss, D. A.: Der Zusammenhang zwischen Poltern und Stottern. *Folia Phoniatrica, 2:* 252, 1950.
45. Wise, R. A.: Personal Communication, March 8, 1955.

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CONTRIBUTION TO THE KNOWLEDGE OF ACUTE BRAIN DEATH[1]

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In patients of a general hospital, with various diseases other than those of the central nervous system, there are some cases which suddenly and unexpectedly develop grave acute neurologic symptoms and die within a few hours or days. Since July of 1945 we have examined 30 cases of this type. Clinically these represent an heterogenous group out of which we have selected two in order to demonstrate the clinical and the histological features of what is commonly known as "acute brain death." The histological examination was carried out with silver carbonate and revealed extensive destruction of the brain (ameboid degeneration of the glia or clasmatodendrosis).

Case I (Lab. No. 14484) D. R., a white girl, aged 12, was admitted on 9-10-53. Five months previously she had developed a skin disease which was diagnosed as dermatitis herpetiformis. She was treated at home, but nothing is known of the type of treatment. The child apparently did not completely recover from this condition, and 10 days before admission to the hospital she developed a skin rash which was described as "German measles like" and was associated with a moderate rise of temperature and severe headaches. She became rapidly worse, developed convulsive attacks, and was admitted to the hospital in status epilepticus.

Clinical examination revealed cyanosis, the residual of a dermatitis of undetermined type and bilateral choked discs of approximately 5 diopters. The patient was in coma.

Bilateral trephines showed definite swelling of the brain, but the ventriculogram was normal. One hour after operation decerebrate rigidity developed, the temperature rose rapidly to 104.2, and the child expired during a generalized convulsion.

Post mortem examination. The brain was edematous; on coronal sections the gray matter was well demarcated from the white, and the basal ganglia were well outlined. There were scattered petechial hemorrhages in the white matter. The cerebellum and the brain stem showed no gross pathology.

Histological examination. The most conspicuous change was the degeneration of the oligodendroglia which was transformed into large, swollen, round bodies with the nuclei frequently shifted to the periphery of the cell (fig. 1). Very few cells retained remnants of processes; the spaces between the degenerated oligodendroglial elements were filled with fragments of destroyed cells ("filling bodies"). The astro and microglia showed equally severe destruction, and only a few of these elements, reduced to ameboid state, could still be seen (fig. 2). The neurons showed acute, non-specific degeneration. In the white matter, the neuraxes were markedly rarified, and the fibers which survived were separated by an accumulation of swollen and necrotic glial elements. In the cerebellum the astroglia was proliferated, but there were no ameboid cells.

Case II (Lab. No. 13155) K. B., a white, married woman, 40 years of age, was admitted to the hospital on 9-26-50. She was well until October, 1949, when she had an attack of what was considered pleuritis which was, however, associated with generalized edema of the skin, especially of the face, hands and feet. There were also nausea, abdominal discomfort and a moderate elevation of the temperature. There were periods when the patient appeared semistuperous. The fever lasted only 4–5 days, and the edema disappeared within 3 weeks. Four months later she complained of generalized pruritus, but there was no skin erruption. These symptoms also gradually subsided. In June of 1950, following a slight injury to the hand, she developed a generalized lymphangitis with fever which was followed by generalized edema and pains in the chest and extremities. This attack was less severe than the two previous ones had been. Laboratory studies at that time revealed a leucopenia

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[2] From the Neuropsychiatric Institute, University of Michigan, Ann Arbor, Michigan. Grant in Aid from the U. S. Department of Health and Welfare.

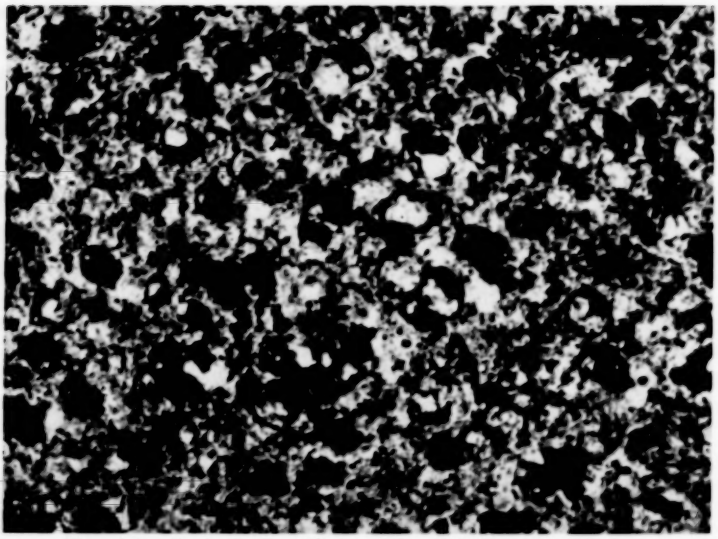

FIG. 1. Severe swelling of the oligodendroglia with destruction of their processes the remnants of which (filling bodies) fill out the spaces between the cells. Microphotograph × 500.

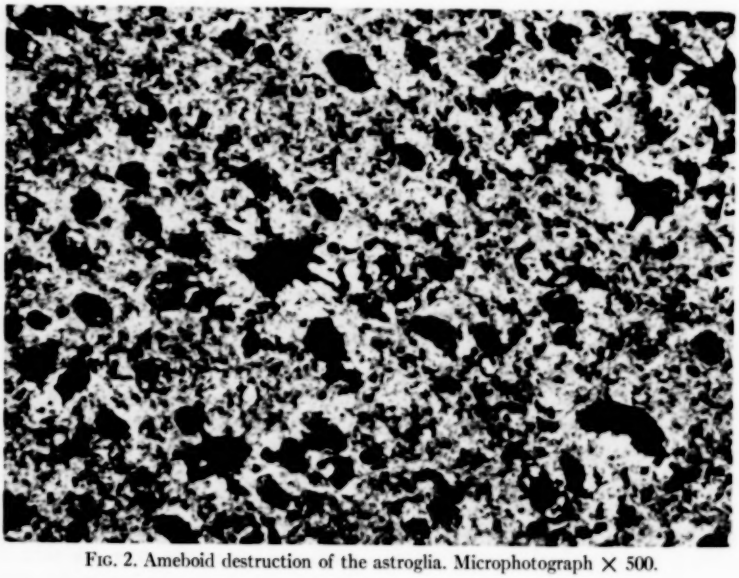

FIG. 2. Ameboid destruction of the astroglia. Microphotograph × 500.

with a white blood cell count of 1,300. She gradually improved but complained of general malaise and easy fatigue.

On 9-22-50 pains in the chest again appeared and persisted until the time of admission 4 days later. The patient stated that she had been easily fatigued for the past 3 years, was sensitive to colds and described symptoms comparable to Raynaud's syndrome.

Physical examination. The patient was a well-developed and nourished female; her temperature was 100, pulse 104, respirations 20. Her skin was distinctly pigmented, the nail beds were slightly cyanotic, mucous mem-

branes were pale. Posterior cervical and several axillary nodes were hard and moderately swollen. Ophthalmoscopic examination showed bilaterally three white exudates, half the size of the disc, in the region of the inferior and superior temporal vessels above and below the macula, but the patient did not complain of impairment of vision. The origin of these exudates remained obscure. The blood count showed 10,400 white cells with 72 per cent neutrophils and was otherwise normal. Other laboratory examinations were within normal limits.

The patient complained of fatigue and of pain in the left shoulder, but she was otherwise relatively comfortable. Eleven days after admission her temperature rose to 101, with severe chills, and there was vertigo, nausea, abdominal discomfort and emesis; the skin became cold and clammy; she was unable to speak but understood questions and answered by shaking her head. Within 24 hours the patient became comatose, perspired profusely, had several generalized convulsive attacks and expired.

Post mortem examination. There was moderate edema of the brain but no other gross changes. Histological examination of the organs of the body showed only a marked increase of the thyroid stroma and reduction in numbers and size of the acini. There was also a small colloid adenoma. These changes were interpreted as suggesting a Graves constitution thyroid, which had been treated with iodine and which had become a hypothyroid state. The histological examination of other organs of the body revealed nothing of significance. The skin was normal (Dr. C. V. Weller, Department of Pathology).

Cortex. There were numerous areas of necrosis in which the glia were so disintegrated that it was difficult to determine the nature of destroyed cells (fig. 3). Judicious application of numerous variants of the silver carbonate technique showed that all types of glia were similarly affected. The neurons were markedly degenerated, but these changes were non-specific.

In the white matter the dominant histologic phenomenon was the pre-ameboid and ameboid state of the astroglia (fig. 4). The astrocytes were hypertrophic; their processes were swollen and broken into fragments; there was moderate swelling of the oligodendroglia. The vessels were surrounded by necrotic cells (fig. 5); the neuraxis was rarified, swollen and fragmented.

In the cerebellum the majority of the Purkinje cells were destroyed, and there were

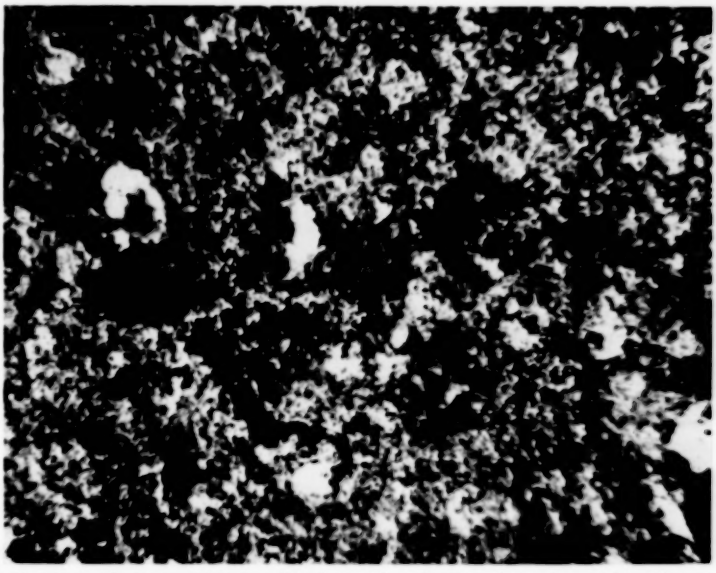

FIG. 3. Necrotic area in the cortex with complete destruction of cells and structures. Microphotograph × 500.

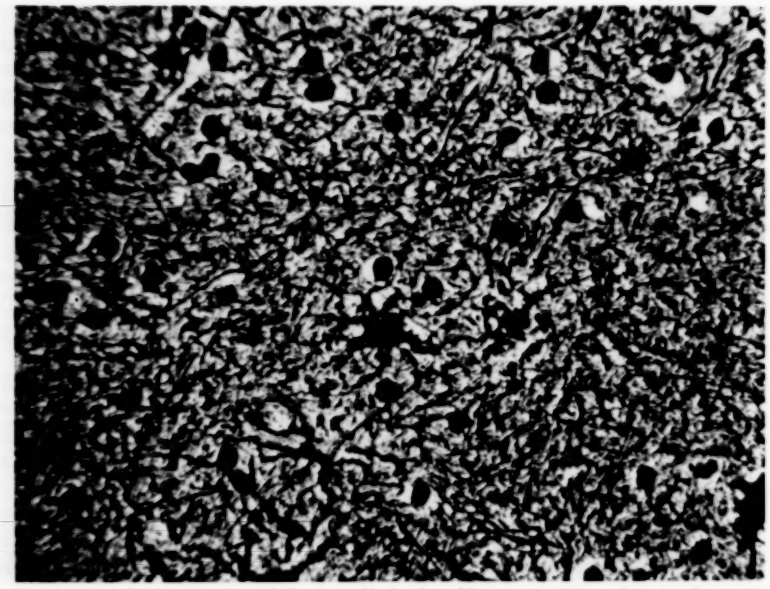

FIG. 4. Ameboid degeneration of the astroglia in the white matter. Microphotograph × 500.

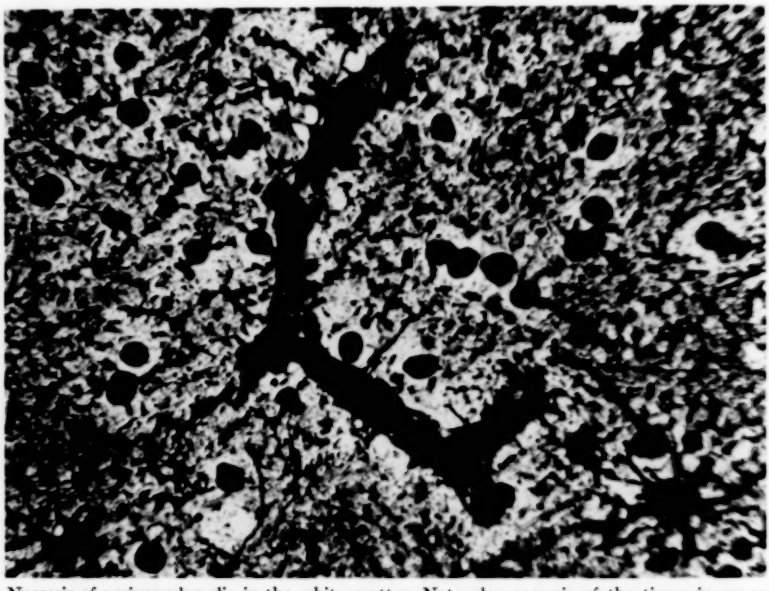

FIG. 5. Necrosis of perivascular glia in the white matter. Note also necrosis of the tissue in general. Microphotograph × 500.

numerous empty baskets; the plexi of the molecular layer were destroyed. The neurons of the granular layer, the mossy fibers and the glomeruli were reduced in number; the astroglia of the white matter was in a pre-ameboid state.

Comment. Ameboid disintegration of the glia was described by Alzheimer (1) in acute and

chronic diseases of the nervous system. In initial stages he found proliferation of the glia with numerous mitoses which was followed by destruction of the processes and swelling of the body of the cells which resembled amebas. According to Alzheimer ameboid cells are morphologically different from "fully developed forms" and are extremely numerous in the white matter. They are surrounded by fragments of their processes, so called "filling bodies," which fill out the space between the destroyed structures. Alzheimer (1) found ameboid degeneration in acute exacerbation of general paresis, in acute "toxic psychosis" and in convulsive disorders. He concluded that this type of glial response always occurred in previously irritated tissue and indicated severe damage.

The silver carbonate technique facilitates investigation of the glia in biopsy and autopsy material and augments the findings of Alzheimer. Further studies of this pathologic phenomenon with silver carbonate have been reported by del Rio Hortega (2) and by Scharenberg (3), who were able to confirm the conclusions of Alzheimer.

The two cases here described represent different phases of ameboid degeneration; the first is characterized by an acute irritation and destruction of nerve tissue, which is in accord with the fulminating clinical course. The most conspicuous change is the swelling of the oligodendroglia which overshadows the destruction of other types of cells. In spite of nearly complete destruction of the oligodendroglia of the hemispheres of the brain, the response of the tissue in the cerebellum remained limited to proliferation and beginning tumefaction of the astrocytes; the parenchyma remained virtually intact. In the second case the histologic findings reflect a more chronic course. The predominant finding in the white matter is the pre-ameboid disintegration of the astroglia and scattered foci of necrosis. In the cortex, on the contrary, destruction of the glial structures is more advanced, and there are numerous areas of necrosis. The histologic character of the degeneration in the cerebellum is different from that in the cerebrum; affected are the elements of Purkinje, basket cells and their fiber systems, the climbing and mossy fibers and neurons and glomeruli of the granular layers, but the response of the glia is less marked.

Ameboid degeneration is a common phenomenon and occurs in a wide variety of disorders, in some of which the nervous system is not primarily involved. This is found in a number of conditions such as convulsive disorders (temporal lobe epilepsy) in which it is almost constant, in acute and chronic catatonic states, in disturbances of metabolism—such as uremia, some forms of diabetes, in toxic conditions (peritonitis, ulcerative colitis), in allergic states (asthma), in virus diseases (poliomyelitis, herpes—case I), in obscure diseases of body and brain (case II), following major surgery, severe head trauma and many others. The histologic picture is therefore nonspecific and does not indicate the etiology. This type of degeneration may be compatible with life for a number of years. In biopsy material from the frontal lobe in a case of catatonic stupor of 13 years' duration, severe ameboid disintegration of all types of glia associated with chronic degeneration of the neurons was reported by one of us (3). At the present time 3 years after removal of a part of the right frontal lobe, the patient is still living, and her condition has not changed. It would appear therefore that essentially the same type of degeneration of the brain may be consistent with life, even though the patient has characteristic, far-advanced, organic brain syndrome. The clinical significance of this pathologic phenomenon lies in its frequent occurrence and dubious prognosis.

Summary

We have presented two cases of brain death, one showing pathologic evidence of an acute, the other of a more chronic process. We have also mentioned biopsy material from a patient who has survived some 3 years after removal of tissue showing similar changes. No explanation as to the metabolic factors involved which result in these changes is offered.

BIBLIOGRAPHY

1. Alzheimer, A.: Beiträge zur Kenntnis der pathologischen Neuroglia. *Histologische und Histopathologische Arbeiten, 3:* 401, 1910.
2. del Rio Hortega, P.: Ensayo De Clasificacion De Las Alteraciones Celulares Del Tejido Nervioso. *Arch. de Histologia Normal y Patologica, 2:* 37, 1943.
3. Scharenberg, K.: Histopathology of catatonic states. *J. Neuropathol. & Exper. Neurol., 13:* 592, 1954.

PSYCHOLOGICAL PROBLEMS OF PATIENTS WITH MYASTHENIA GRAVIS

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This study represents an attempt to understand the adjustment problems and emotional difficulties experienced by patients suffering from myasthenia gravis. It is assumed that a better understanding of the nature of the problems which patients with this illness face will be helpful in the therapeutic approach to them.

Our interest in this study was stimulated when an adolescent girl with myasthenia gravis was referred for psychiatric treatment. This patient remained in therapy for 16 months. To add to the information and insights gleaned during this period, an unselected group of 12 patients under treatment in the Neurology Clinic at the Neuropsychiatric Institute of the University of Illinois was seen for detailed anamnestic interviews.

Many of the difficulties in living which are faced by patients with myasthenia gravis are common to other chronic illnesses. There are, however, some which are specific for this syndrome.

For discussion purposes the information gathered during interviews has been subsumed under headings. The first is the reaction to the information presented by the physician about the disease. The second is the response to the continuous need for medication. The third is a consideration of the problems of adaptation to the stress of this illness.

According to Grob and Harvey (1): "The factors associated with exacerbation of the disease were most commonly upper respiratory infections, emotional tension and the post-partum period." Since "emotional tension" is a broad term, an effort was made to ascertain if non-specific upsets would produce an increase in symptoms or if only specific psychological situations would do so.

Reactions to Information about the Disease

All of the patients in this series had been told the name of their illness, once the diagnosis was established, but two claimed they were given no information about the nature of the process. Since patients were not familiar with the term myasthenia gravis, it carried none of the impact of words like "cancer" or "polio." One woman initially was pleased to have a label applied to her illness because she thought "If the doctors know what's wrong with me, they will be able to do something for me." Later she became severely depressed when she read a popular magazine article in which it was stated that myasthenia gravis was incurable.

Once the diagnosis was stated, the patient was usually told three additional facts: 1) that the disease is chronic (or long lasting), 2) that it is treatable but not curable, and 3) that, like for diabetes, medication would have to be taken indefinitely.

It is important for the physician to discuss these points with the patient. Now-a-days information—good and bad, accurate and inaccurate—can be obtained from popular periodicals. It is less traumatic to receive unpleasant facts when someone is standing by to provide support than it is to obtain them from cold print. Also, the elements of hope can be stressed, and personal anxieties (not covered in the magazine article) can be handled. Secondly, since sustained treatment is necessary for a prolonged period or for the duration of life (as it is with glaucoma and diabetes mellitus), it is necessary to explain the rationale for therapy to obtain participation in a program in which the patient is helped to help himself.

The manner in which patients reacted to the information which was imparted to them depended upon the way in which they were told, the severity of the process, and their previous personality makeup. One patient said: "I just gave up hope when I was told about my illness, and I did not want to know anything more about it." Her outlook changed, however, when she showed demonstrable improvement with treatment. Another patient searched the medical literature to find a cure which she could suggest to her physicians. This woman, who had previously had five abdominal operations,

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urgently requested a thymectomy. A third woman became somewhat euphoric and remained so. She stated that she was certain that her illness was not like those in textbooks, and therefore it would disappear. She maintained this attitude even when (or probably because) medication did not relieve her diplopia and ptosis.

The full impact of the diagnosis and the explanations is not always absorbed at once. The reaction may be deferred or fractionated much like it is when a beloved person dies. One man was not "hit" until a year after he had received considerable information about his illness. The impact occurred when he saw the diagnosis spelled out on an insurance form. Until that time he had partly warded off his feelings by the defenses of denial and isolation.

Thus far we have discussed the reactions to the facts that patients should be told. We should also consider the reactions to facts which they should *not* be told. The teen-aged girl, who first focused our attention on myasthenia gravis, had gathered much information about her illness by unobtrusively listening to the physicians when they made their ward rounds. She had learned that the process was more serious in adolescents than adults, that some newer medications could not be used to treat her because if they did not work she might not respond to prostigmine, and that patients of her age could suddenly "go into crisis" and die. This information markedly (and unnecessarily) intensified her fears.

Reactions to Medication

The patients interviewed were all treated with prostigmine, but the dosage ranged from 15 mg. three times a day to 15 mg. hourly around the clock. For the most part it was taken orally, but in some instances it was given by hypodermic injection. Sufficient information had been imparted to the patients to enlist their active participation. It was understood that the drug would have to be taken indefinitely.

During the interviews the patients spontaneously talked about their treatment program. As would be expected, the responses to this program revealed information about the patients' personality makeup and attitude, and it reflected their total adjustment to the illness.

The responses varied greatly. There was one woman who turned over the responsibility of her treatment to her children although physically she was able to handle it herself. She used her illness to justify a marked emotional regression. She welcomed a housekeeper and felt "good" when anyone took care of her. Despite ptosis of her eye lids and difficulty in chewing, she would forget to take her medication unless she was reminded. For others who neglected to take prostigmine occasionally, the symptoms of the disease served as a reminder for appropriate action.

In contrast to this woman, another patient went to great lengths to deny her illness and her dependent feelings. She decreased her dosage or neglected to take her prostigmine. She "drove" herself, striving to work in spite of difficulty in holding objects in her hands. This was in keeping with her life-long pattern in which work had always played an important part in sustaining an emotional balance.

Unlike the first two women, a third not only took her medication regularly, but she regulated her dosage to meet changing conditions and needs. She regarded this as a common sense approach. Her great fear when she was told about her illness was that it would preclude marriage and childbearing. After she married and had a child, her general outlook improved, and she required less medication. Accordingly, she reduced the dosage. When her requirements increased after very heavy work, she would temporarily increase the dosage. It is our impression that an attempt at self-regulation, based upon an understanding of the illness and within the general framework of the physician's prescription, indicates active participation in a process of rehabilitation.

A patient who used denial as an important defense said that she felt depressed every time that she had to take her pills because they were a reminder of her illness. At other times, so she stated, she tried to "kid" herself and to believe that she was not sick at all.

A patient who used compulsive defenses stated that the focus on time which resulted from her treatment schedule (four times a day) pervaded her whole life to the point that she felt that everything was regulated by the clock.

A man, who had had myasthenia gravis for 35 years, stated that it was reassuring to him to know that he could get medicine. It had saved his life once. He went on to say that he

would be afraid only if he could not get medicine, but then he modified this by saying that if he knew he had enough medicine for the rest of his life, but was told that he could not come to the clinic, he would still be afraid. He clearly brought out the fact that while he relied upon medication, the support derived from physicians was necessary to combat the fear and anxiety engendered by his illness.

Thus far we have discussed the information which can be gleaned from the patients' reactions to the treatment program. These were highly individual and revealing. The response to a change in dosage prescribed by a physician had a more universal quality and was anxiety-producing for almost all patients. An increased dosage usually was interpreted as an indication that there had been an "onward march" of the disease. A decrease in the dosage raised the question: Will this amount control the symptoms?

Stress and Adaptation

A disease like myasthenia gravis which is disabling will frequently mobilize, aggravate or bring to light conflicts about dependency feelings. Concepts of normality, stability or flexibility have relatively little meaning when we consider the adjustment or adaptation to an illness. People with intense longings to have others care for them may tolerate an invalided state with few emotional repercussions. They often respond poorly, however, to efforts at rehabilitation. Conversely, persons who struggle against having others take care of them will react poorly when they are incapacitated. They are more apt to respond favorably, however, to a program of rehabilitation. The meaninglessness of a concept of normality in relationship to physical limitations can be brought out most clearly by an analogy. A hermit-like man marooned on a desert island will endure his isolation with more equanimity than a gregarious man. Obviously this has nothing to do with normality, stability or flexibility.

In our series of patients, one woman accepted dependency with little conflict. In fact, she used the illness as a justification for expressing previously concealed yearnings. To do this she magnified the extent of her helplessness. This was the woman who would not take her medicine unless reminded to do so by her children. She did less and less about her home and had a housekeeper take over for her. Although she had worked until the time of her illness, she was frank in stating that she did not miss her job.

Another patient was just as willing to accept dependency, but he was not as fortunate in finding people who would gratify his desires. He was a 65-year-old man, whose hostile-dependent relationship with his wife had finally culminated in a divorce. He openly stated that if he had had a leg amputed or if he were blind, people would understand that he was disabled. They would then pity him and be willing to help him. He bewailed the fact that it was his fate to have an illness which did not show. People did not understand what it was to have myasthenia gravis, and so they thought he was lazy or "crazy." He finally decided that he would speak about his condition only to physicians because only they were capable of comprehending his plight. He did his best to dramatize his state. At the start of the interview his handshake was weak and flabby, but when he was distracted and less intent upon making an impression, it was firm and strong. Although initially his voice was thin and whiney, it became full and resolute when he pleaded his case. He turned his tears off and on at a moment's notice, and he emoted like an actor in an old time melodrama. Although he was reluctant to speak at first, stating that he had been advised not to use his voice very much, it was difficult to terminate the interview once he was wound up.

Unlike these first two patients, a third patient found it very trying to endure the dependency imposed by her illness. She was a 22-year-old woman who had a twin sister. This sister had used illness as her way of obtaining special consideration from their mother. The patient would tell her mother that the sister was "putting on." She always thought that "half of it was in the mind." She, on the other hand, received special consideration for being a hard worker. The patient stated: "When my mother wanted something done, she would ask me because she knew that even if I didn't want to do it I still would." She had continued to run a small business even after her marriage and the birth of a child, but she was forced to give it up when she became ill. Her attitude was

epitomized by the statement: "I can't just sit and watch TV. I have to sew or get something done at the same time. That's just the way I am." As the result of her illness there was a disparity between her emotional drive and her physical capacity. She became very aggravated when she wanted to do a task but did not feel up to it. In spite of her weakness, she would persevere until she had completed the job. In the morning when she first awakened, she experienced the most disabling symptoms and with it the most intense irritability. She would take her medication, remain in bed for about 2 hours, and then with the return of strength and energy her outlook would improve. For this patient the specific symptom of weakness interfered with the pattern of being the doer or worker although she waged a somewhat desperate and often frustrating battle to maintain some of her previous activity.

A patient who was unable to accept her own attitude of self-pity (and perhaps longed for this response from others), expressed a strong dislike for her family's attitude which she regarded as one of pity even though she knew it was not. Prior to her illness she had prided herself on her self-sufficiency and her ability to support herself and her daughter. She became less depressed when her response to medication made it possible for her to do her own housework.

In one instance physicians were directly involved in a patient's dependency problem. A man reacted badly to his first physician's injunction that he return to work. He felt that the doctor made it sound as if it were his fault that he was ill. When he said that he was unable to return to his former employment, the physician seemed to be angry. When he was transferred to a second physician after about a year, he was depressed. He ate little but drank much alcohol. The second physician suggested that the patient go to work but at a lighter job, and he offered to write a letter for him. The patient responded well to this and obtained an office job. He had formerly done heavy work in a machine shop. He cut down on his drinking, his appetite returned, and his feeling of depression lifted. He said that it was a good thing that he was back at work because his home situation was worse than ever. His parents did very little for him. "They are foreign," he said, "and don't understand what this (his illness) is all about." It seems apparent that he reacted to the first physician in the same way that he responded to his parents. Neither accepted the physical limitations and intensification of dependency needs (needs for understanding, support, etc.) produced by his disease. The second physician accepted his illness (and the needs which went with it), and with this help he responded well.

Thus far we have considered the dependency problems of patients who are confronted by an illness which partially incapacitates them. A second factor is that of fear and anxiety and depression engendered by the threat to the integrity of the body and to life. Obviously in a real sense, it is impossible to separate one factor from another, but for the sake of discussion we have done this.

Euphoria was a prominent mechanism of defense for one patient. She had felt "high" from the time she was told about her disease. She became extremely active in community work, and she tended to keep her life geared at a general rather than an individual level. Thus she thought in terms of the community rather than of a member of a group and of the clinic rather than of one physician. Although she wore the mask of a happy and cheerful person, traces of an underlying depression showed through during the interviews.

A man, previously mentioned, combated his fears by his faith in medication and in physicians. He also used diversion as a prominent mechanism.

In our series the patient who was most profoundly ill was the adolescent girl who focused our attention on the reactions to myasthenia gravis. Her illness had begun with weakness of both legs. Within a period of months the process had progressed to the point that there were severe bilateral lid ptosis, weakness of all four extremities and difficulty in chewing, swallowing and speaking. On two occasions within a one-year period she had to be placed in a respirator because of a respiratory crisis. When first seen by one of us (M. B.), she had recently been discharged from the hospital. She was taking medication every hour around the clock (alternately by mouth and by hypodermic). She was able to walk alone although awkwardly, and she could speak for brief

periods of time. She was a girl of better than average intelligence, and she previously had not suffered from manifest neurotic symptoms. She had been told by her neurologist that it was not known how long she would have to take medication and that there was no way of predicting when her symptoms would clear up. No other direct discussion of the prognosis had been presented to her. She had overheard conversations, however, during ward rounds in which it was stated that the illness had a rapid course in younger people and that she probably had about 1 or 2 years to live. After a short period in treatment (on a once a week basis), she became interested in doing a number of things which were within her physical limitations. She took up sewing and clay modeling, and she started an aquarium. As she became more secure in her relationship with the therapist, she expressed some of her fears. It was then that she recounted the various things she had overheard while in the hospital. During one of her visits, she made a rowboat out of clay, and in it she placed a human figure. For the boat she made only one oar. She provided the person with some provisions. Her fantasy was that the person was out on a large ocean and unable to swim. She spoke of the fact that she had been a good swimmer before her illness. It was apparent that she was the person in the boat—with one oar, undoubtedly an expression of half-hope and half-hopelessness. This graphic picture of her plight certainly brought out the fact that she was in a situation which was dangerous and in which she was at least half helpless. In spite of this she was able to derive considerable support from the medical and psychiatric treatment she received. She was able to resume taking her meals with her family and to continue her schooling with a teacher who came to her home. It was not until 2 weeks before her death that she became depressed and spoke of a feeling of hopelessness. This was about 2 months before the 2-year period was up—the period of life expectancy mentioned at the hospital.

Thus far we have considered the problems which arise because of the intensified needs for help and the threat to life which arise with an illness like myasthenia gravis. As in all illnesses, we found that some patients interpreted the process in the light of the emotional problems which were pressing at the time. This was most striking in the case of an adolescent girl who confessed that she had had sexual intercourse once—shortly before she became ill. She stated that someone in her neighborhood had started a rumor that the disease from which she suffered was like syphilis. She had been an extremely active person, dated a great deal, and had a strong group identification and spirit. She felt that the illness had deprived her of everything she liked, and she regarded it as punishment for having been a "bad girl." She missed her former activities with her friends, and she felt that she was excluded more because there was something wrong with her as a person than because she was physically handicapped.

The most distressing symptom in our series of patients was that of generalized weakness. Only one person was upset about her unsteady gait. She thought that people might think that she was drunk. It is entirely possible, and even likely, that patients who have a special investment in an organ or who view it in a symbolic way might have a profound reaction to diplopia, ptosis, weakness of the masticatory muscles and symptoms of myasthenia gravis involving other organ systems.

As would be expected in any trying situation, there are always people who will find constructive features in a destructive process or, to put it another way, will make a virtue out of a necessity. This process was most poignantly described by a patient suffering from another disfiguring and disabling affliction who said that he was the type of person who could find beauty in a swamp. The woman who was afraid that myasthenia gravis would interfere with marriage and child raising brought out the fact that if it had not been for her illness, she would not have been as happy as she was. It had forced her to look into herself and to take a more serious view on life. Although this was, at least partly, a rationalization, it was possibly more than that.

On the basis of our observations, we are unable to make any statement about how the patients viewed themselves in their dreams, and whether or not the focus on the musculoskeletal system was accentuated.

Emotions and Symptoms

With one exception every patient interviewed had noted a cause and effect relationship between being upset and an increase in physical symptoms. The one exception was the woman who became euphoric at the onset of her illness. She maintained that she was able to "ignore" anything which might be upsetting to others and that nothing influenced her symptoms.

The word "upset" is a general one which may refer to many dissimilar feelings. We wondered if the nature of the emotion which increased the symptoms was more specific. On the basis of our observations, it seems that only when anger or envy is provoked is there an adverse physical response.

The reaction to anger was striking in some situations which we were able to observe directly. One man, who objected to being interviewed, became so incapacitated that the interview had to be terminated. His speech became nasal and unintelligible and his lids began to droop. The adolescent girl, who was seen on a therapeutic basis, became provoked and verbalized some of her anger when an ash tray she had made was lost by the occupational therapy department. She then became very weak. From that time on she refused to go to occupational therapy. There were other instances in which she avoided anger-producing situations at home. For example, when her brothers and sisters began to misbehave, she would go to her room. Parenthetically, we can state that the avoidance of anger-producing situations may be an appropriate defensive maneuver for the patient with myasthenia gravis.

The twin, whom we have discussed, found that any situation which made her feel "aggravated" increased her feeling of weakness. One man experienced diplopia, which he compared to seeing red, whenever he had an argument with his wife. Another patient found that her symptoms became more marked whenever her children fought.

The words "upset" or "excitement" usually meant anger, but occasionally they meant envy. One woman found that she could not tolerate seeing a group of her friends having a good time. She would have to go off by herself because the mounting feeling of envy would be followed by an increase in the severity of her symptoms. The woman, who was fearful that her illness would prevent her from marrying, became severely distressed emotionally and physically at the time of her brother's marriage.

Our data do not permit definite conclusions either as to the specificity of the emotional reactions responsible for the production of an intensification of symptoms or as to the mechanism which underlies the process. In our study we have noted that anger and envy mobilize an adverse physical reaction. It is apparent that this is not due to increased sympathetic nervous system activity since ephedrine either alone or in combination with prostigmine relieves the symptoms of myasthenia gravis. Secondly, sexual excitement has no marked influence. It seems likely that the adverse reaction is due to the impulse to muscular action and its inhibition. This would be similar to the toll taken by heavy physical exertion.

Summary

1. Patients who suffer from myasthenia gravis are usually told the diagnosis and given some information about the nature of their illness. The name itself carries none of the impact of "polio" or "cancer". Hence there is less fear. Hope can be engendered both verbally and concretely (i.e., through the effect of medication).

2. Much information about the patient's adjustment to the disease can be obtained from the patient's attitude toward taking medication. This has been illustrated with brief notes from our anamnestic data.

3. Much of the patient's adjustment to the illness can be understood in terms of the reactions to 1) fear and 2) dependency. A third consideration is the patient's interpretation of the process based on the emotional problems which existed at the time of its onset. In some instances there may be specific problems based on the involvement of an organ that has special meaning to the patient.

To a limited degree myasthenia gravis is a two-phase illness. There are the phase of disability and the phase of rehabilitation. The

latter starts when medication is given. Obviously the problems—especially those of dependency—are different in the two phases. This difference is largely the result of the previous personality makeup of the patient.

4. The symptoms of myasthenia gravis are intensified by "emotional upsets". These more specifically seem to involve anger and envy. Their effect is possibly a direct one on the skeletal musculature.

BIBLIOGRAPHY

1. Grob, D., and Harvey, A.: Abnormalities in neuromuscular transmission with special reference to myasthenia gravis. *Am. J. Med.*, *5*: 695, 1953.

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INTRACRANIAL NEOPLASMS MASKED AS DEPRESSIONS AND DIAGNOSED WITH THE AID OF ELECTROENCEPHALOGRAPHY[1]

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Karl Kleist more than any neuropsychiatrist has pointed out the occurrence in patients with cerebral disease of all the various symptoms and syndromes commonly encountered in the so-called functional psychoses. His work extends almost over half a century. Not only did he meticulously describe many symptoms and syndromes of the psychotics, but he also collected a large amount of clinical-anatomical material to demonstrate the close association of a number of psychiatric pictures with lesions of well-defined cerebral structures (1–8). Quite aside from the great theoretical impact of this work, it should remind us constantly that any kind of psychiatric syndrome may appear in the course of organic brain disease and that no psychiatric diagnosis should be made withoug careful neurological study, even if the psychiatric syndrome shows none of the criteria of an organic mental syndrome.

The following four cases will demonstrate the necessity of careful neurological examination in cases of depression and will also show that in some cases clinical neurological examination alone will not prove the presence of an intracranial lesion, without the additional use of laboratory methods as e.g. electroencephalography.

Case 1: This 58-year-old French woman was seen by me first on November 13, 1953. Since 1951, she readily fatigued, and this was explained by endocrine disturbances and family problems. Her blood cholesterol had been found to be elevated. For this, she was put on a diet, advised to rest, and given numerous injections of male and female sex hormones. During the last few months she complained of disagreeable sensations around her heart and expressed the fear that she had a serious heart disease. During the last two months she complained that she could not read as well as before, i.e., had difficulties in understanding what she read. She also said that she could not write as before and that her memory was bad. For three weeks she has had headaches all over her head, lack of appetite and occasional slight nauseousness.

At the first interview, the patient was in a state of agitated depression. She was in severe despair, felt that she was very sick, could not fulfill her duties and would be better dead. She repeated her complaints incessantly, and it was extremely difficult to interrupt this recitation and to make her answer any specific questions. She was completely oriented and showed no memory defect for remote or recent events. Neurological examination had an entirely negative result. In particular, there was no evidence of aphasia, apraxia, alexia, agraphia, acalculia.

It was felt at that time that the patient suffered in all probability from involutional melancholia. However, in view of the unusual complaints about difficulties in reading and writing, she was asked to return the next day for an electroencephalogram. This record showed a focus of delta activity with frequencies as low as 0.8 cps. at the left temporal electrodes with much slow activity also at the left occipital electrode. A diagnosis of a left posterior temporal lobe tumor was made. After discovering a focal lesion by electroencephalography, the visual fields were rechecked immediately, and a homonymous cut was found in the right upper quadrant. The patient was subsequently operated on in France, and a large gliogenous tumor was found in the left temporal lobe. Details of localization and histological structure have not been available.

Remarks: This patient gave the impression of having an involutional depression with many hypochondriac features. Headaches, bad memory, lack of appetite and nauseousness are not unusual complaints in these psychoses while complaints about difficulties in reading and writing are less common. On the other hand, many depressive patients state that they cannot concentrate on their reading matter and are unable to understand the content. Therefore, it seemed possible to interpret the reading difficulties in this manner. However, the combination of this complaint with the other somatic complaints prompted further investigation and led to the discovery of a focal lesion by electroencephalography. Only after an electroencephalographic focus had been found, did the repeated and more careful perimetric examination reveal the visual field defect.

Case 2: This 43-year-old man was first seen by me on March 21, 1945. During the last 3 years he had worried about difficulties in his business. More lately, he had

[1] Dedicated to Professor Karl Kleist on the occasion of his 75th birthday.

[2] From the Neurological Service of Dr. M. B. Bender, The Mount Sinai Hospital, New York City.

also been worried about the expected induction of his son into the armed services. He has always been an "emotional" man, easily depressed when there were any difficulties. Seven years ago he had had a depressive state lasting 3 months. During the last years he has complained increasingly that his wife did not give him enough assistance and affection. He has been quite depressed during the last 3 months. Now he cries much, does not feel adequate to his work, cannot concentrate, makes mistakes on more complicated arithmetic problems, has occasional headaches, and thinks that his memory is not as good as before. One year ago he "fainted" twice following excitement. He was not completely unconscious but could hear what was said. These episodes were diagnosed as being hysterical by his physician at that time.

On examination, he showed a depressive syndrome with lack of self confidence, indecision and some slowness of all responses. There was no disturbance of orientation and memory, no dyscalculia. Neurological examination had an entirely negative result. A diagnosis of manic-depressive depression was made, and he was given Benzedrine sulfate. He felt very much better with this medication and was not seen again in April and May. In June he called by telephone and complained that his memory had become much worse and that he sometimes did not know which day it was. He was advised to return for reexamination on June 3, 1945. At this time there was no objective disturbance of orientation or memory. Neurological examination revealed bilateral papilledema but was entirely negative otherwise. An electroencephalogram was taken and showed a focus of very slow high voltage activity in the right frontal region. After this result had been obtained, the neurological examination was repeated with particular attention to minor signs on the left side. This led to the discovery of slight drifting of the left arm and slightly more active patellar and suprapatellar reflexes on the left side. These findings were so minimal that the neurosurgeon, who examined him later, was not at all convinced of their significance. The patient was hospitalized. X-rays of the skull showed decalcification of the dorsum sellae and the posterior clinoid processes. The vascular markings in the right frontal region were "perhaps slightly exaggerated". On operation by Dr. Ira Cohen a metastatic carcinoma was found deep in the right frontal lobe. The patient died a few days later. On autopsy, after long searching, the primary tumor, smaller than a pea, was found in the lung.

Remarks: This patient, aside from his last depressive episode, had had a similar condition in 1938. This, together with the negative neurological status, led to the diagnosis of a true psychosis. It was felt that the complaints about bad memory and headaches were part of the depressive state, and it seemed probably that the previous "fainting" was due to emotional causes. Although in June, 1945, the diagnosis of intracranial disease was made on the basis of the papilledema, the electroencephalogram localized the lesion and led to the discovery of minor neurological deviations which had been overlooked before.

The following two cases were referred primarily for electroencephalography. Therefore, less information on them is available than on the first two cases.

Case 3: This 55-year-old physician was referred for electroencephalography because he continued to complain about a disturbance of memory since he had had a series of electric shock treatments terminated 3 months ago. The electroencephalogram was supposed to determine whether the disturbance of memory was a complaint due to his depressive state or caused by the electric shock treatment. I was not given a complete history, but I was told that the patient had been emotionally unstable for many years and that he had been depressed for 3 years. He had been treated with psychoanalysis and electric shock. During the last 2 years he had also complained about headache, diagnosed as migraine, and during the last few days about a disturbance of balance.

The electroencephalogram showed a very severe focal disturbance with frequencies as slow as 1 cps. in the right frontal region. After subsequent neurological examination, which revealed slight left-sided weakness with increased reflexes, and after cerebral arteriography a large right frontal parasagittal fibroblastic meningioma was removed by Dr. Leo M. Davidoff. On discharge from the hospital, 5 weeks after the operation, the depressive state was no longer present, and there was no neurological deficit except for a left foot drop.

Remarks: In this patient, the persistent complaint of disturbed memory finally led to the discovery of a brain tumor by electroencephalography after the patient had been treated with psychotherapy and electric shock for over a year.

Case 4: This 52-year-old doctor's wife, first seen by me on December 2, 1952, had always been a rather serious person and afraid of sickness all her adult life. In 1946, she started to have repeated periods of depression, lasting from several weeks to several months. She was seen by numerous physicians and was always found to be organically well. In April, 1952, she was given six electric shock treatments, after which she was better. However, during the summer she got worse and in August, 1952, attempted suicide with an overdose of barbiturates. During this entire period, the diagnoses of various physicians had been either hysteria or manic-depressive depression. Complaints about headaches, nausea, and vomiting, a strange sensation on the right side of the face, and complaints about increasing deafness in the right ear, all of which had appeared during the last 6 months, were considered to be part of the psychiatric disorder.

She was brought to me by her family physician for an electroencephalogram as it was felt that one should

prove to her by a normal electroencephalogram that there was really nothing wrong with her head. The electroencephalogram, however, showed diffuse and symmetrical 4 to 6 cps. activity, more at the occipital than at the other electrodes.

An immediately following neurological examination revealed: right-sided papilledema, complete nerve deafness on the right side, absent right corneal reflex, right trigeminal hypesthesia, very slight right facial weakness.

The behavior of the patient was of great interest. When she arrived at the office, she was in complete despair. She said that she was terribly sick, that nobody believed her, and that she just did not want to live anymore under these conditions. She described her manifold complaints with many words. After the diagnosis of acoustic neuroma had been made, the husband did not want the patient to be told as he feared that she might react with an even more severe emotional disturbance. As, however, the patient had to be given a reason for the necessary hospitalization, she was told that she had in all probability an intracranial tumor and that there was a good chance that it could be removed completely. Upon this information, her behavior changed abruptly. She became almost cheerful, showed no panic of any kind, consented readily to hospitalization and operation.

With the diagnosis of right acoustic neuroma, she was admitted to the neurological service of the Mount Sinai Hospital. After further studies, a large acoustic neuroma was removed by Dr. Leo M. Davidoff on December 11, 1952. The operation left her with a peripheral facial palsy and with considerable ataxia. In spite of these disturbances, the patient has been in good spirits ever since, has taken up her social life and shown no signs of depression whatsoever.

Remarks: The organic intracranial disease could, of course, have been discovered without electroencephalography which was performed for a really not valid reason. Again, as in the other cases, the physical complaints were overlooked in their significance and considered as part of the depression.

Comment

These four patients were diagnosed as depressions while an intracranial neoplasm was overlooked. Two patients (3 and 4) had received electric shock treatments. In two patients (1 and 2) careful neurological examination seemed to have an entirely negative result. In one of them (2) papilledema appeared later. In addition, in both these patients minor neurological signs could be found after the electroencephalogram had directed the attention in a definite direction. Case 4 presented definite neurological signs, when seen by me, and it remains unknown how long before the examination some such signs had been present. Case 3 was never examined by me but showed positive neurological signs when seen the next day at the hospital. In these two last cases, therefore, the intracranial disorder was discovered by neurological examination after the abnormal electroencephalogram prompted a repeated neurological evaluation, similar to the cases recently described by Waggoner and Bagchi (1).

Of course, the diagnosis of organic brain disease is obvious if one encounters an organic mental syndrome with disturbances of orientation, memory and state of consciousness. Three of the four patients complained about a disturbance of memory which, one might argue, should have raised the suspicion of organic brain disease. However, none of these patients showed evidence of a true disturbance of memory on examination. Also, the complaint of bad memory is commonly heard in depressive psychoses. This complaint reflects often the lack of attention for outside events or is an expression of the self-deprecatory attitude of the patient. Headache was complained of in all four cases, nausea in two. Both are complaints not uncommon in the true depressive psychoses.

On the other hand, all patients had some complaints which are unusual in non-organic depressions. Case 1 complained about difficulties in reading and writing. Case 2 had had fainting spells. Case 3 complained about a disturbance of balance; case 4 about unilateral deafness and facial dysesthesia. Each patient, therefore, had at least one complaint, unusual in true depressive psychosis. This should have warned the examiner, including myself, to study the patient most carefully for the presence of intracranial disease. One should use at least all the innocuous laboratory methods (X-rays, electroencephalography) in all cases where such unusual complaints are brought forward, in particular if there are additional complaints about a disturbance of memory and headache.

Aside from the unusual positive symptoms, there was also the absence of some symptoms commonly seen at least in the manic-depressive depressions. Only one of the patients (case 1) had some self reproaches, and only one

patient (case 2) complained about retardation of his thought processes.

Recently Schlesinger (10) in a very comprehensive paper has reviewed the mental changes in patients with intracranial tumors. In none of the 591 cases was there a psychosis diagnosed as melancholia or manic-depressive. Only 26 of the patients, which is less than 5%, showed depression, most of them having tumors involving the frontal lobe. We quote these numbers to show that depression so far seemed to be relatively rare in patients with intracranial tumors. This may be one of the reasons that the diagnosis of intracranial tumor is not considered often enough in patients with depressive syndrome. This is also manifest from Moore's (9) series of 10 cases of "clinically unrecognized meningiomas", 2 of which were diagnosed as involutional depressions.

The question of the localization of the lesions in relation to the mental syndrome, also discussed extensively by Schlesinger, cannot be discussed on the basis of four observations. However, one has to realize that the lesion by itself does not "explain" the depression but that the particular type of psychiatric picture is rather the result of the reaction of the patient to the organic disorder, a point that has recently been stressed by Weinstein and coworkers (12). In this respect, it is interesting to note that cases 2 and 4 had always shown depressive trends and had suffered from overt depressions previously and that case 3 had shown emotional instability for a long time. One might conclude, therefore, that a rather unspecific generalized disturbance of brain function, as caused by the expanding lesion, brought to the fore a type of reaction to which the patient was inclined due to his personality make-up. However, such an explanation does not account for the special features of case 4, where the depressive state disappeared after the patient was told that a tangible cause for her somatic complaints had been found. In this case, at least three factors are evident, none of which can be exempted from having played a part in the genesis of the depressive state: 1) the personality make-up, 2) the diffuse disturbance of brain function as shown by the electroencephalogram, and 3) the desperate situation created by the presence of physically caused complaints which everybody, contrary to what the patient could accept, blamed on psychological factors.

In spite of the above, it seems unjustified to postulate that the localization of the cerebral lesion is of no significance for the production of a certain mental syndrome even if one agrees that this mental syndrome is the resultant of personality factors, environmental factors and the disturbance of brain function caused by the intracranial disease. Only further studies, taking into account all these factors, including localization, type, rate of progression and distant effects of the focal cerebral process, will elucidate this problem.

Whatever the particular relation between the depression and the intracranial lesion may have been in the various cases, the intracranial tumor should have been diagnosed before administering psychiatric treatment, including electric shock. It is hoped that this paper will assist in avoiding similar mistakes in the future.

Summary

Four patients with intracranial tumors are described which had been diagnosed and treated as depressions and in which the diagnosis of intracranial neoplasm was made with the aid of electroencephalography. Some of the factors, operative in creating depressive states in patients with intracranial tumors, are discussed.

BIBLIOGRAPHY

1. Kleist, K.: *Untersuchungen zur Kenntnis der psychomotorischen Stoerungen bei Geisteskranken.* Leipzig: Klinkhardt, 1908.
2. Kleist, K.: *Weitere Untersuchungen an Geisteskranken mit psychomotorischen Stoerungen.* Leipzig: Klinkhardt, 1909.
3. Kleist, K.: Die psychomotorischen Stoerungen und ihr Verhaltnis zu den Motilitaetsstoerungen bei Erkrankungen der Stammganglien. *Monatschrift f. Psychiatrie u. Neurologie, 53:* 253–302, 1922.
4. Kleist, K.: Wesen und Lokalisation der Paralogie. *Zentralblatt f. die gesamte Neurologie u. Psychiatrie, 33:* 1923.
5. Kleist, K.: Gegenhalten (motorischer Negativismus), Zwangsgreifen und Thalamus opticus. *Monatschrift f. Psychatrie u. Neurologie, 65:* 317–396, 1927.
6. Kleist, K.: Psychomotorische Stoerungen, Caudatum und Pallidum externum. *Zentralblatt f. die gesamte Neurologie u. Psychiatrie, 47:* 1927.
7. Kleist, K.: Bewegungsstoerungen und Bewegungsleistungen der Stammganglien des Gehirns

(Myostase und Psychomotorik). *Naturwissenschaften, 15:* 973–977, 1927.

8. Kleist, K.: Kriegsverletzungen des Gehirns in ihrer Bedeutung fuer die Hirnlokalisation und Hirnpathologie. In: von Schjerning, O., *Handbuch der aerztlichen Erfahrungen im Weltkriege 1914–1918*, vol. 4, 343–1416. Leipzig: Barth, 1934.
9. Moore, M. T.: The fate of clinically unrecognized meningiomas. *Neurology, 4:* 837–856, 1954.
10. Schlesinger, B.: Mental changes in intracranial tumors. *Confinia neurol., 50:* 223–355, 1950.
11. Waggoner, R. W., and Bagchi, B. K.: Initial masking of organic brain changes by psychic symptoms: Clinical and electroencephalographic studies. *Am. J. Psychiat., 110:* 904–910, 1954.
12. Weinstein, E. A., and Kahn, R. L.: Personality factors in denial of illness. *Arch. Neurol. & Psychiat., 69:* 355–367, 1953.

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CHLORPROMAZINE FOR THE CONTROL OF PSYCHOMOTOR EXCITEMENT IN THE MENTALLY DEFICIENT

A Preliminary Study

JUDITH H. RETTIG, M.D.

The findings of Lehmann and Hanrahan (2) who studied chlorpromazine in 71 hospitalized psychiatric patients revealed that this drug is of unique value in the symptomatic control of almost any kind of severe excitement. They were particularly impressed with the favorable results in manic depressive patients, all of whom had been continuously manic or hypomanic for more than a year and had previously failed to respond to standard therapeutic procedures or had had only brief remissions. The study of Sheatz (3) brought out that patients with irreversible brain damage who were extremely overactive were successfully quieted with relatively small doses of chlorpromazine. Moreover, Elkes and Elkes (1) from a trial of the drug in patients from the disturbed wards of the Winson Green Hospital, Birmingham, England, reported that their patients had become quiet, responsive and less destructive.

Since our review of the literature indicated that there was little or no published information on the use of chlorpromazine in mentally deficient patients, we undertook this evaluation to assess its usefulness in controlling psychomotor excitement in such patients.

Material and Methods

For the study, 27 mentally-deficient patients—5 males and 22 females—whose chronological age ranged frum 14 to 64 years, were selected from the population of Columbus State School. The clinical characteristics of these patients are summarized in table 1. All were highly disturbed, hyperactive, and violent. They were destructive to their surroundings and clothing, screaming and uncontrollable. Some had to be restrained almost continually; others had to be secluded for long periods of time. Temper tantrums were frequent, often accompanied by self-injury, threats of suicide, assaultiveness against the staff and other patients. Several patients actively experienced hallucinations and delusions and were disoriented as to identity, time, and space. The problems of soiling were great. Duration of custodial care ranged from 7 months to 19 years, with an average of 5 years.

Intelligence quotients determined by commonly used tests, including the Stanford-Binet and Wechsler-Bellevue, indicated that of the 24 mentally-deficient patients tested, 12 were judged to be high-grade (I.Q. 70-51), 6 middle grade (I.Q. 50-31), and 6 low-grade (I.Q. 30 or under). Of the remaining three patients, two were tested using the Vineland Social Maturity Scale and showed social quotients of 17 and 27, respectively. One patient could not be tested because of her hyperactivity.

All of the patients selected for this study failed to benefit from previous treatment which included barbiturates, electroshock therapy, occupational therapy, and psychotherapy. They remained manageable only with extreme difficulty—a burden to themselves as well as to those who cared for them.

When chlorpromazine[1] therapy was started, all other medication was discontinued. Initially, 25 mg. to 50 mg. were given intramuscularly, augmented by 25 mg. to 50 mg. orally, as needed to maintain the patient calm. Once under control, they were switched to oral medication in doses of 25 mg. to 50 mg., usually four times daily.

The dose for each patient was tailored to give optimal results, increased or decreased, so as to establish a level of behavior in which control was possible without resorting to barbiturates, restraints, or seclusion.

All patients but one have received chlorpromazine for more than 6 months. The exception is a patient who reacted with severe depression necessitating withdrawal of the drug.

[1] 10-(3-dimethylaminopropyl)-2-chlorphenothiazine hydrochloride supplied as Thorazine by Smith, Kline and French Laboratories, Philadelphia, Pennsylvania. It was originally developed in France by Rhone-Poulenc-Specia Laboratories who market it abroad and in Canada as Largactil.

Results

Table 1 summarizes our results with chlorpromazine in managing disturbed mentally-deficient patients. The efficacy of the drug was judged on the basis of the following criteria: (a) degree of cooperation; (b) absence or presence of destructiveness; (c) habit training; (d) disposition; (e) sleeping habits. Persistence at a given task and initiative were taken into account when differentiating between "excellent" and "good" results.

An *excellent* result was characterized by complete cooperation of the patient with the staff and with fellow patients, a cheerful disposition, absence of soiling and destructiveness, normalization of sleeping habits, and little need for supervision because of a certain amount of initiative and persistence at a given task. The result was judged *good* when there was a clear-cut improvement in the physical management of the patient, that is, the disappearance of destructiveness, soiling, and generally, of hyperactive behavior. Patients, in whom results were judged to be *fair*, became tidy and manageable for lengthy periods of time although occasionally there were relapses to overactive and destructive behavior—with the need for restraining them. *Poor* results were judged when only transient, non-recurring betterment in manageability or, in one case, adverse side-effects occurred necessitating discontinuance of therapy. When there was no perceptible change in the clinical picture of the patient, the results were graded *none*.

Using these criteria, results in this series of 27 patients were judged as *excellent* in 8 patients, *good* in 11, *fair* in 4, *poor* in 2, and *none* in 2. The failures occurred mostly in those patients who had suffered severe brain injury and in whom large areas of the brain were actually destroyed.

The changes which our units have undergone since the introduction of chlorpromazine into the regimen are marked. Generally speaking, most hyperactive patients who had been extreme conduct problems became quiet, manageable and cooperative. At night almost all slept well. As temper tantrums occurred with much less frequency, the need for isolation and restraint was virtually eliminated.

With the patients calm and more receptive to their social environment, more efficient training and rehabilitation are possible, or, at least, more efficient custodial care can be carried out for those with extensive brain damage. Some of the institutional personnel released from the time-consuming duty of disciplining and restraining overactive patients may be employed more profitably in recreation, in the training of patients, and in ways more profitable emotionally to themselves. On the whole, this and the savings resulting from less destruction make for a better balanced institutional economy.

Case Histories

The following case histories illustrate some of the typical results obtained with chlorpromazine:

Side Effects

Case 1: J. B., a 15-year-old girl, was admitted on May 24, 1954, because of severe disorderly behavior in the community. She was found to be a borderline mental defective, familial, with behavioral reaction. Her I.Q. measured by the Wechsler I test was 71. In the various cottages where she lived, the patient was labeled by the nursing attendants as "uncontrollable" and "unmanageable". Her frequent temper tantrums provoked altercations with the other girls and, in general, upset the unit and its routine. She was constantly in motion, jumping through windows, walking the floor at night, playing hide-and-seek, and so on. The other girls expressed thorough dislike for her, and even the attendants, who were inured to such behavior, hesitated to tangle with her unless aided by other personnel.

On October 18, 1954, she was placed on chlorpromazine therapy and reacted with an almost remarkable improvement of behavior. She became quiet, easily managed, cooperative, and attentive to other patients, particularly those who were physically handicapped. She showed interest in her surroundings and in the school in which she was placed. Today she is progressing well with her school work. Moreover, her matron describes her as a constructive helper in her cottage, the attendants comment on her cooperativeness, and her companions find that she has become more sociable and they in turn have become friendly to her. At present she is being maintained on 50 mg. orally, t.i.d. and has sustained her improvement.

Case 2: G. S., now a 29-year-old woman, suffered a fractured skull in an automobile accident when she was 14. Shortly afterward her behavior changed markedly in that she became unruly, high-tempered, nervous, wandered about the house, and was unable to sleep. She grew progressively worse, until, three years later, it became necessary to confine her to an institution. Her condition was diagnosed as chronic brain syndrome associated with trauma, brain trauma-gross force, with neurotic reaction, with mental deficiency.

Since her admission she has had a long history of bizarre behavior, self-inflicted injuries, temper tantrums, sullenness, and antagonistic behavior toward at-

TABLE 1.—Clinical Data of 27 Patients in Study of Effect of Chlorpromazine Therapy

Patient	Age	Sex	I.Q.	Diagnosis	Length of Institutionalization	Behavior before Chlorpromazine	Behavior after Chlorpromazine Treatment	Results in Terms of Manageability
J. B.	15	F	71	Familial c̄ behav. react.	7 mo.	Destructive, screaming incessantly	Quiet and cooperative	Excellent
M. L. R.	16	F	17*	Idiopathic c̄ psych. react.	20 mo.	Restive, unruly	Sleeps well, manageable	Fair
M. G. T.	32	F	27*	Familial c̄ psych. react., c̄ convul.	18 mo.	Surly, untidy	Better disposition, grooming	Good
M. O'G.	33	F	11	Familial c̄ psych. react.	4½ mo.	Hyperactive; in restraint	Some restraint still necessary	Fair
L. H.	20	F	63	Familial c̄ psych. react.	16 mo.	Manic, hyperactive	Severe depression	Poor
E. A. W.	17	F	30	Idiopathic, severe	4½ yr.	Violent, screaming	Less tense	Fair
T. C.	46	F	62	Idiopathic c̄ psych. react.	15 yr.	Hyperactive, destructive, irritable, with temper tantrums	Quiet, more occupied, relaxed	Excellent
I. K.	41	F	61	Idiopathic c̄ psych. react.	7 yr.	Disorientated, violent	Quiet, cooperative, less psychotic	Good
G. S.	29	F	44	Brain injury c̄ neurotic react.	12 yr.	Sullen, self-injurious	Pleasant, and cooperative	Excellent
M. W.	16	F	14	Idiopathic c̄ catatonic react.	22 mo.	Hyperactive, mute, unmanageable	Communicative, happy, and cheerful	Good
E. C.	30	F	59	Familial c̄ schizophrenic react.	19 yr.	Too unruly for ward	Calmed, no seclusion needed	Excellent
J. E.	19	F	54	CBS c̄ intracranial infection	10 yr.	Fighting, secluded from others	Quiet; no need for seclusion	Excellent
D. A. L.	19	F	40	Familial c̄ psych. react.	3 yr.	Manic, unruly	Quiet, manageable	Excellent
P. C.	19	F	48	Familial c̄ behavioral react.	2½ yr.	Violent, in seclusion	Manageable, relaxed	Excellent
J. L. McN.	14	F	23	CBS c̄ intracranial infection	4 yr.	Babbling, tense	Speech coherent, quiet	Fair
E. G.	64	F	33	Iodiopathic c̄ behavioral react.	21 mo.	Soiler, truculent	Tidy, helpful, good; slight depression	Good
J. E.	15	F	†	Psychotic disorder c̄ hebephrenic react.	3 yr.	Self-abusive, assaultive	Quiet and cooperative. On "trial" visit home	Excellent
D. S.	15	F	38	Idiopathic c̄ behavioral react.	4 yr.	Temper tantrums with destructiveness	Tantrums less frequent, quiet, manageable	Good
T. A. J.	16	F	65	Idiopathic c̄ psych. react.	4 yr.	Anti-social; frequent tantrums	Manageable and cooperative; temper tantrums much less frequent	Good
M. A. W.	23	F	62	CBS c̄ psych. react.	10 yt.	Aggressive, moody	Manageable and cooperative	Good
G. S.	31	F	64	Familial c̄ behavioral react.	11 yr.	Trouble-maker, aggressive	No change	None
A. U.	33	F	57	Familial c̄ behavioral react.	2½ yr.	Suicidal	Quiet, less introspective	Good
W. B.	17	M	73	CBS (birth trauma) c̄ behavioral react.	2 yr.	Combative, obscene, and sadistic	Quiet and a bit more manageable; at times friendly and cheerful	Good

D. R. McK.	14	M	20	CBS (constitutional influence) c̄ congential plegias and behavioral react.	3 yr.	Disoriented, mute; restraints needed on occasions	Quiet; restraints not necessary	Good
R. A. McC.	16	M	5	CBS (birth trauma) c̄ behavioral react.	3 yr.	Facial grimaces, hyperactive, destructive	No change	None
R. L. T.	23	M	10	CBS c̄ behavioral react.	4 yr.	Agitated, spastic flexion of left forearm and hand	No change	Poor
N. S.	17	M	40	CBS (birth trauma) c̄ behavioral react.	7 yr.	Alternately hyperactive and depressed	Quiet and cooperative	Good

* Social quotient.
† Resisted testing.

tendants and other patients in her cottage. At times she would refuse to eat; in cold weather she would run outside scantly clothed and there parade flauntingly or lie on the ground. Barbiturates had very little effect on her behavior.

This patient was first given chlorpromazine on October 20, 1954. She responded to the drug immediately and improved remarkably. At present she is a cottage worker and doing a better than average job of helping physically handicapped patients. She has shown considerable initiative in performing numerous errands with little or no direction, in helping the cottage physicians with the preparation of patients for injections, and so on. She is pleasant, cooperative, capable, and has become a useful member of the institutional society. Her present maintenance dose of chlorpromazine is 50 mg., orally, t.i.d.

Case 3: T. C., a woman now 46-years-old, was first admitted to a mental institution 15 years ago when she became acutely disturbed, violent, and destructive. Psychological testing revealed mental deficiency with psychotic reaction. Although the patient was known to have been mentally-deficient since birth, she had managed to get along fairly well in the community, working about the house and creating no particular problems. When her mother died, however, her behavior changed for the worse, and 4 years later she had to be committed to a state hospital. She was later transferred to Columbus State School where she has remained since 1942 except for one year's stay at a sanatorium, when she was found to have active tuberculosis. Because of temper tantrums and destructiveness she had to be secluded often. Even when not secluded her periods of hyperactivity and extreme irritability were frequent; she avidly sought the attention and sympathy of the attendants and, with equal vigor, fought frequently with other patients.

In January, 1954, the patient began to express bizarre ideation, depersonalization, and seemed to be hallucinating both auditorily and visually. Between February 17 and March 24, 1954, she received 26 electroshock treatments resulting in improvement; that is, she no longer had bizarre ideas although her destructive behavior persisted. Sedatives produced only slight behavioral improvement. Chlorpromazine therapy was therefore instituted on October 20, 1954, and resulted in rapid behavioral improvement. The patient could be easily managed and was helpful around the ward. She no longer required seclusion at any time for her manifestations of hyperactivity or irritability. Consequently, the patient was permitted to go home for a trial visit—*the first time in 15 years*. It proved highly successful, and the patient's family reported that she was a model of good behavior during her stay at home. She was returned to the hospital, greatly delighted about her progress, and apparently quite content with the thought that she would be permitted future visits at home.

Drowsiness, which proved to be the principal side effect, was considered more helpful than disadvantageous in these hard-to-manage patients. Usually it was transient and subsided after the first few days of therapy.

Other side effects were rare: Two patients complained of anorexia; one, of vomiting. The case of severe depression following chlorpromazine therapy has already been mentioned. Another patient became slightly depressed but her over-all response was good. She became tidy, helpful on the wards, and friendly in contrast to her former slovenly, irascible, and churlish behavior.

Summary and Conclusions

Twenty-seven highly disturbed, mentally-deficient patients were treated with chlorpromazine (25–50 mg., four times daily) for a period of 6 months. Results were judged excellent in 8, good in 11, fair in 4. Four patients did not respond to the drug. Results were best in those patients whose disturbance was primarily emotional in nature, that is, the greater the actual brain damage, the less the effectiveness of the drug. Generally speaking, chlorpromazine was highly useful in bringing about better manageability of overactive and destructive patients.

The impact of the drug on the attendants personally and administratively was equally important. Relieving them of time-consuming duties, chiefly custodial and disciplinary, permitted them to spend more time in therapy and has consequently raised their morale considerably. With less destructiveness and through better manageability, maintenance costs should be reduced.

Side effects were minimal and consisted principally of transient drowsiness, which was considered an asset with these overactive patients. Two patients complained of anorexia; one, of vomiting. In one patient it was necessary to discontinue the therapy because she became depressed.

The author wishes to thank Myra Chatters, M.D., and Willa Caldwell, M.D., without whose help this study could not have been done.

Bibliography

1. Elkes, J., and Elkes, C.: Effect of chlorpromazine on the behavior of chronically overactive psychotic patients. *Brit. M. J., 11:* 560–565, 1955.
2. Lehmann, H. E., and Hanrahan, G. E.: Chlorpromazine; New inhibiting agent for psychomotor excitement and manic states. *A.M.A. Arch. Neurol. & Psychiat., 71:* 227–237, 1954.
3. Sheatz, G. C.: Studies on chlorpromazine in decerebrate dogs and patients with irreversible brain damage. *J. Pharmacol. & Exper. Therap., 113:* 47a, 1955.

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PLASMA TYROSINE IN SCHIZOPHRENIA[1]

JAMES ENGLISH MILES, M.D.[2]

Introduction

There is no evidence that tyrosine is directly implicated in schizophrenia. Individual amino acids were studied by Pond (9) in various forms of mental disorder as well as in normals by means of paper partition chromatography. In chromatograms of cerebrospinal fluid and plasma he found no significant differences in normals and schizophrenics. In his study tyrosine was only visualized occasionally but was not otherwise remarkable.

Osmond and Smythies (8) have pointed out the structural similarity that exists between the alkaloid mescaline and epinephrine. These authors feel that mescaline, in its effects on the human subject, reproduces many of the features of an acute schizophrenic picture to a greater or lesser degree. They note in agreement with Hoskins (4) that disorders of the adrenosympathetic system are regularly seen in schizophrenia together with abnormal responses to drugs acting on the autonomic system. Osmond and Smythies (8) suggest the theoretical possibility that a metabolic disorder of the transmethylation process could lead to methylation of one or both of the phenolic hydroxyl groups of epinephrine, producing a compound related structurally and pharmacologically to mescaline; and this compound is postulated as the etiological agent in schizophrenia. Noteboom (7) and DeJong (1) have studied various phenylalanine derivatives closely related structurally to both mescaline and epinephrine; several of these agents have produced catatonia-like pictures and affective reactions in animals more marked than mescaline.

Since evidence suggests that tyrosine is the metabolic precursor of epinephrine (2), it was thought that the logical point to attack the problem was to study tyrosine itself. Alterations of tyrosine metabolism on a genetic basis have been described in a number of diseases characterized as "inborn errors of metabolism" (6), such as tyrosinosis, alkaptonuria, phenylketonuria, and albinism; and at least one (phenylpyruvic oligophrenia) has been shown to be accompanied regularly by mental changes. The purpose of the present investigation is to determine quantitatively the values for fasting free plasma tyrosine in a group of schizophrenics and normal controls of similar age, and to compare spectral-transmittance curves obtained by the colorimetric method used in the two groups.

Methods

Subjects: The experimental subjects were 32 chronic male schizophrenics, aged 28 to 54, hospitalized for four years or longer. Sixteen normal males, ranging in age from 24 to 57 years, were control subjects.

Samples: Twenty cc. of blood were drawn from each subject in the post-absorbtive state after a fast of twelve hours. Coagulation was prevented with oxalates. The samples were spun down under constant conditions (4,000 rpm. for 30 minutes) within one hour after collection, and the plasma was pipetted off and frozen for storage.

Determinations: The method used for tyrosine determination was that of Udenfriend and Cooper (10). For each series of determinations, experimental and control samples were run simultaneously together with a standard and a reagent blank. Four determinations were made for each subject. Known quantities of l-tyrosine were carried through the procedure, and a standard curve was obtained. Quantification was achieved by reading the experimental values on the standard curve at 450 mμ.

The results of this colorimetric method were read in the Coleman Junior Spectrophotometer at intervals of 5 mμ from 400 to 700 mμ and plotted directly as per cent transmittance against wavelength. Mean curves for each individual and each group were obtained.

[1] The author is greatly indebted to Samuel Friedman, M.D., Assistant Superintendent of the Fairfield State Hospital, Newtown, Connecticut, for kindly providing the clinical material, and to Paul Kunkel, M.D., Chief of the Medical Service, Veterans Administration Hospital, West Haven, Connecticut, for making laboratory facilities and technical assistance available.

[2] Now at the Veterans Administration Hospital, Long Beach 4, California.

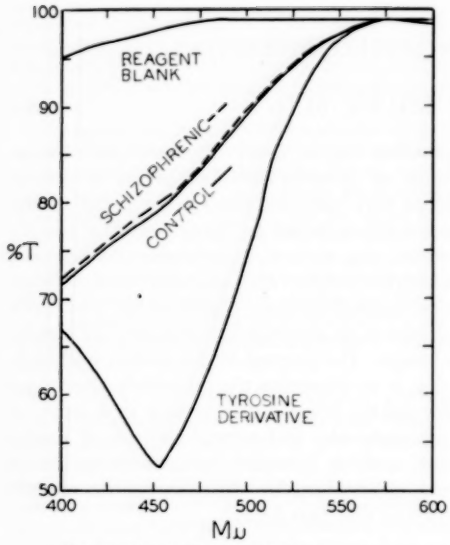

FIG. 1. Spectral-transmittance curves

The curves represent mean values for each group in terms of per cent transmittance plotted against wavelength in mμ.

RESULTS

The mean value for free fasting plasma tyrosine in schizophrenic subjects was 12.4 μg. per cc. ± 2.6 (S.D.). The mean control value was 13.5 μg. per cc. ± 2.0 (S.D.). Mean values for each of the four diagnostic categories, simple, hebephrenic, catatonic and paranoid, were compared in the schizophrenic group and did not differ appreciably from one another.

These figures are in good agreement with those of Hier and Bergheim (3), who determined levels of free plasma tyrosine in normal men by a microbiological method, obtaining a mean value of 15.0 μg. per cc. ± 3.7. Johnson and Bergheim (5) also determined free plasma tyrosine levels microbiologically in normal men, obtaining a mean value of 10.5 μg. per cc. ± 2.0.

The mean Spectral-Transmittance (S-T) curves for schizophrenics and controls are presented in figure 1, together with mean standard and reagent blank curves. Curves for individual samples were found to be highly reproducible. No mean curve, based on four determinations for any individual, experimental or control, differed considerably from the over-all mean curve for his group.

It is noted in figure 1 in agreement with the observation of Udenfriend and Cooper (10) that spectral curves for human plasma differ considerably from the curves obtained when a sample of pure l-tyrosine is carried through the procedure.

As shown in the figure there was no overlap between reagent blank curves and the experimental and control curves.

DISCUSSION

The results of this study suggest that there is no significant difference in the fasting levels of free plasma tyrosine in chronic male schizophrenics when compared to control subjects of similar age.

The fact that mean S-T curves in both schizophrenic and control groups were nearly superimposable suggests that the chromophores did not differ quantitatively or qualitatively in these groups since Udenfriend and Cooper (10) have shown that the spectral curves are highly dependent on the chromophores involved.

The fact that the curves in the two groups differed altogether from the curve obtained when l-tyrosine was carried through the procedure suggests that other chromophores than tyrosine were involved in the reaction. Udenfriend and Cooper (10) note that tryptophan and glycine, but no other amino acids, give faint colors with nitrosonaphthol. They note also that many substituted phenolic compounds such as tyramine react to give strong colors. This may mean that substituted phenols comprising the intermediate metabolites of tyrosine and phenylalanine are involved in the reaction with human plasma to give the curves obtained in this study since these amino acids are the metabolic source of such phenols (10). Comparison of these substituted phenols by means of their chromophore representatives on the S-T curves thus may allow a comparison of some intermediate metabolites of tyrosine as well as the amino acid itself. The fact that the mean S-T curves for the schizophrenic and control groups were nearly superimposable with no individual curve differing significantly from the mean for his group suggests therefore that the intermediate metabolism of tyrosine is not deranged in schizophrenia. These findings do not support the hypothesis that a

specific disorder of metabolism involving the chemistry of tyrosine may underlie schizophrenia.

SUMMARY

1) Determinations of free fasting plasma tyrosine were made on 32 chronic male schizophrenics and 16 male controls of similar age.

2) There was no significant difference in the values for free fasting plasma tyrosine when the schizophrenic group was compared to the control group. Figures for both groups were in agreement with accepted values.

3) The Spectral-Transmittance (S-T) curves of chromophores obtained by the colorimetric method used were plotted for each subject between 400 and 700 mμ.

4) Mean S-T curves for schizophrenics and controls did not differ significantly, and no individual gave curves which differed significantly from the mean curve for his group. Since substituted phenols other than tyrosine, presumably representing intermediate metabolites of tyrosine, are involved in the reaction of the method used, producing colored compounds which affect the S-T curve specifically, the results suggest that the intermediate metabolism of tyrosine is not deranged in schizophrenia.

5) The results obtained do not support the hypothesis that schizophrenia may represent a state of disordered metabolism involving the chemistry of tyrosine.

BIBLIOGRAPHY

1. DeJong, H. H.: Die Experimentelle Catatonie also vielfach vorkommende Reaktionsform des Zentralnervensystems. *Zeitschr. f. d. ges. Neurol. u. Psychiat., 39:* 468, 1932.
2. Harper, H. A.: *Review of Physiological Chemistry.* Third Edition, pp. 214. California: University Medical Publishers, 1951.
3. Hier, S. W., and Bergheim, O.: The microbiological determination of certain free amino acids in human and dog plasma. *J. Biol. Chem., 163:* 129, 1946.
4. Hoskins, R.: *The Biology of Schizophrenia.* New York: W. W. Norton and Co., 1946.
5. Johnson, C. A., and Bergheim, O.: The distribution of free amino acids between erythrocytes and plasma in man. *J. Biol. Chem., 188:* 833, 1951.
6. Nelson, W. E. (Editor): *Mitchell-Nelson Textbook of Pediatrics,* pp. 283 ff. Philadelphia: W. B. Saunders, 1950.
7. Noteboom, L.: Experimental catatonia by means of derivatives of mescaline and adrenaline. *Proc. Royal Acad. Sc. Amsterdam, 37:* 562, 1934.
8. Osmond, H., and Smythies, M. B.: Schizophrenia: a new approach. *J. Ment. Sc., 98:* 309, 1952.
9. Pond, M. H.: Some studies of the amino acids in body fluids in patients with various forms of mental disease by paper partition chromatography. *J. Ment. Sc., 96:* 1048, 1950.
10. Udenfriend, S., and Cooper, J. R.: The chemical estimation of tyrosine and tyramine. *J. Biol. Chem., 196:* 227, 1952.

ANTIHISTAMINE TREATMENT OF ALCOHOLISM

MORTON M. STERN, M.D.[1]

In 1948 following reports of the use of antihistamines in drug addiction, studies were initiated to determine the effects of antihistamine treatment upon alcoholic patients in the author's private practice. Since that time a group of six men and five women have been treated among whom were two schizophrenics, one involutional patient and nine non-psychotic compulsive drinkers characterized by feelings of inadequacy and tension. Each patient was given 50 mg. of pyrilamine maleate three times a day orally for 1–21 days and followed as much as individual cooperation permitted. Other antihistamines were not tried.

All 11 patients reported a loss of desire for compulsive drinking. One patient on a spree stopped drinking immediately after receiving 0.5 cc. of pyrilamine maleate intravenously. (One schizophrenic patient stated she stopped drinking for fear of mixing alcohol and medication. When she voluntarily reduced medication, she relapsed. Because the difficulty in evaluating this response was greater than is usual with alcoholics, she was considered not to have responded to the medication directly.)

After being placed on medication all patients became clear-eyed, showed no overt evidence of drinking and were free of the stilted mannerisms exhibited by steady drinkers who otherwise maintain a good front. Appetite was not affected adversely except in one patient. Another patient reported an unaccustomed craving for sweets and better tolerance of alcohol. At least six patients where follow-up was at all possible relapsed into compulsive drinking. Three of these relapsers started drinking after being on the same dose for two or three weeks. The others began compulsive drinking at varying periods after discontinuance of treatment. Almost all refused medication eventually and broke contact.

One patient had nausea, vomiting and vertigo after one day of medication, but although treatment was discontinued, objective improvement occurred and she did not drink for one week.

Discussion

In many emotionally maladjusted individuals compulsive drinking once initiated may continue because of secondary autonomic and metabolic imbalance. In a patient taking a drink for social reasons or to overcome feelings of inadequacy or frustration, alcohol may produce histamine-like metabolites as in other individuals. Drinkers, however, having learned to use alcohol as a cure-all for any tension ingest more alcohol for relief from the effects of the metabolites, only to increase still more the production of metabolites. Thus a vicious cycle of ever-increasing histamine-like metabolite production is established by feed-back. The interposition, however, of an histamine antagonist such as was used in this study may break up the cycle by minimizing the effects of the metabolites.

The hypothesis set forth above is strengthened by the report of Sackler *et al.* (2) (published as this paper was being prepared) of decreased craving and increased tolerance for alcohol in histamine treated schizophrenics. The report of beneficial results from the use of ACTH and adrenocortical hormones in alcoholism also seems to point in the direction of metabolic and autonomic imbalance.

The question as to whether there is also a primary or constitutional autonomic and metabolic imbalance was not determined by this study although the high rate of relapse is suggestive of basic factors such as the constitutional.

The possibility that the effects observed were the result of an aversion reaction through stimulation of the emetic center does not seem important since there was no food aversion except in the one patient showing a reaction to the drug. As far as suggestion is concerned, experience shows that alcoholics are usually not amenable to suggestions leading to the withdrawal from alcohol.

There is more likelihood that the observed

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effects may have been caused by sedative action of the pyrilamine maleate. Against this conclusion was the general alertness noted in all patients on antihistamines. This aspect will be investigated further with less sedative antihistamines.

The present incomplete study, as well as the reports by others employing different pharmacological agents (4, 5), illustrates that the determining factor in alcoholism is the personality of the patient. No matter how effective an agent may be in breaking up the immediate drinking cycle, nevertheless no agent to date has been able to satisfy the patients basic needs or overcome the pressure of frustration as well as alcohol. Therefore, the best that a pharmacological agent can be expected to do is to overcome the immediate craving at any one time and perhaps render the patient somewhat more amenable to psychotherapy. Certainly psychotherapy would constitute a more direct attack on the underlying conflicts and defensive formations favoring alcoholic pattern reactions even in a hypothetical constitutionally predisposed individual.

Conclusion

The studies undertaken so far with antihistamine treatment indicate 1) in 10 of 11 private cases the compulsive desire to drink was broken up or averted at least temporarily; 2) the above studies suggest that one factor in alcoholism is the secondary establishment of a backfeeding histamine production mechanism; 3) the role of the antihistamines as shown by these studies is in the treatment of the immediate drinking cycle, whereas the long term role should be carried by psychotherapy.

I wish to express my appreciation to Merck & Company for furnishing the pyrilamine maleate (Neo Antergan®) used in this study.

Bibliography

1. Kells, P.: Pyribenzamine as an adjunct in the control of morphine withdrawal syndrome. *South. M. J., 41:* 134, 1948.
2. Sackler, R. R., Sackler, M. D., Co Tui, Marti-Ibonex, F., and Sackler, A. M.: Tolerance to and craving for alcohol in histamine treated schizophrenics. *Psychiat. Quart., 26:* 597, 1952.
3. Smith, J. J.: *The Role of the Adrenal Gland in Alcoholism.* In Proceedings of the First ACTH Conference, J. R. Mote, Ed., p. 566. Philadelphia: Blakiston, 1950.
4. Beutner, K. R.: Treatment of alcoholism. Mod. Med. *20:* 18, 1952.
5. Diethelm, O.: Advances in the treatment of chronic alcoholism. Bull. N. Y. Acad. Med. *27:* 232, 1951.

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BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Meeting of March 17, 1955

DR. ERICH LINDEMANN, President, *presiding*

THE PATHOLOGY OF PARKINSONISM. *J. G. Greenfield.*

On the occasion of the 200th anniversary of the birth of James Parkinson the speaker discussed the present status of the pathology of paralysis agitans. Lesions in the substantia nigra have been recognized since 1919 as the basis of post-encephalitic Parkinsonism, but the pathology of idiopathic paralysis agitans has been considered in English speaking countries to be more in the corpus striatum and globus pallidus. This view derives especially from the Vogts' (1920) monograph, but their cases were not all typical and their examination of the substantia nigra was admittedly incomplete. Their pupil Hassler (1919, 1937) mapped the normal substantia nigra and found constant loss of certain cell groups in typical paralysis agitans. He also emphasized the presence of hyaline inclusion bodies, first described by Lewy (1913), in the cells of the substantia nigra and locus caeruleus in this disease.

Klaue (1940), Beheim-Schwarzbach (1952), and Greenfield and Bosanquet(1953) have confirmed the constancy of these lesions in the substantia nigra. The later authors differ from Klaue in considering Lewy inclusions characteristic of the idiopathic disease. In post-encephalitic cases they found fibrillary changes of Alzheimer type in the pigmented cells of the brain stem with equal constancy.

Discussion

Dr. Erich Lindemann: This has been a very thought-provoking address. I am sure the members of the group must have thought about specific localization, the nature of the process destroying the nerve cells.

Dr. D. Denny-Brown: I have listened with great pleasure to this paper. Parkinsonism is, I suppose, one of the most difficult problems in neurology from every conceivable aspect, not only from the clinicophysiological aspect, but also the anatomical and neuropathological. There have been many attempts, as you well know, to define one structure, damage to which results in Parkinsonism. Most experimental work has suffered from the over-simplification of our clinical descriptions. The more intense Parkinsonian tremor becomes, the more it involves motion, just as cerebellar tremor in more intense form disturbs posture. Electromyographic studies give no clear-cut manner of defining Parkinsonism from other types of tremor. Study of tremors produced by damaging mid-brain and subthalamic structures convinces one that whatever causes Parkinsonism must be a very diffuse kind of pathology. The classical studies of the neuropathology of Parkinson's disease clearly indicate the diffuse nature of the changes. Which are the primary changes, and which are secondary (transneuronal)? I have long hoped that a neurocytologist of the calibre of Dr. Greenfield would take up this subject. It is clear that he has at once brought into focus the intimate changes in nerve cells and has shown how consistent two types of change reflect the two main types of Parkinsonism. The clinical significance of the prominence of such changes in the substantia nigra and in the locus caeruleus is still not answered. One is immediately reminded of other diffuse diseases of the nervous system such as Wilson's Disease where focal damage does not necessarily account for the dominant symptomatology. Though one has no doubt that these neuronal changes must be primary in this disorder, there still remain problems such as the meaning of the special liability of pigmented cells, and the real nature of these inclusions. Is it possible that the same process affecting the globus pallidus does not produce inclusions only because the cells in that location are not pigmented?

The Lafora bodies in myoclonic epilepsy are also found in the substantia nigra. There is a link between myoclonic epilepsy and Parkinson's disease. In Hassler's paper, the case of Parkinsonism that showed the best inclusion bodies was also a familial one. Therefore if we try to get these inclusions in terms of what we know, it is in terms of these familial diffuse neuronal diseases whose most obvious form is the lipidoses. We still have a long way to go before we can put Parkinson's disease clearly into that category, but Dr. Greenfield's observations point in the direction of this etiology.

Dr. Stanley Cobb: I would like to ask some things. I have always been a little confused about the nomenclature and I think I understand that you use it in the way I do. I would say that Parkinson described the shaking palsy or paralysis agitans. That therefore people who divide the disease into either "paralysis agitans" or "Parkinson's disease" are making a false distinction. If I understand rightly you divide it into two kinds of Parkinson's disease: "idiopathic", the one originally described, and the more recent one that appeared with the epidemics of encephalitis, i.e. "post-encephalitic". If we could agree on how to use this, it would be helpful.

In some brains I looked over with Dr. Benda, we thought there were some significant vascular changes in the striatum and also in the cortex, especially in area 6, and I think we laid stress on the cell loss. You laid your emphasis, rightly from the modern point of view, on these inclusion bodies. Do you believe that the vascular changes are significant? Are the areas of cell loss so general that we need pay no attention to them?

We want to thank you for this clear statement from a pathological point of view. It is hard not to mix in our physiological ideas and fantasies and our surgical ideas. I think the neurosurgeons have, by their experiments on the human, made some interesting observations which we must use in understanding the physi-

ology. This is a disease where animal experimentation will never be satisfactory because the motor apparatus even of the higher monkeys is not the same as in man.

Dr. Paul I. Yakovlev: Would Dr. Greenfield amplify from his experience on the interesting possibility alluded to some 30 years ago by Foix and Nicolesco that in Parkinson's disease the pathologic alterations affect with a certain selectivity the pigmented system of nuclei of the tegmentum: the subst. nigra, locus caeruleus and the chain of pigmented cells scattered in the brain stem. Might Dr. Greenfield be willing to suggest what might be the significance of this curious system of cells "a pigment noir". As Dr. Denny-Brown has just discussed there are indications that Parkinson's Disease may be envisaged as a metabolic disorder of the nervous system. The intracellular inclusions which Dr. Greenfield described to us tonight would seem to point in the same direction. On general grounds one is inclined to consider that the system of pigmented cells in the brain stem as being in some way related to visceral functions and may represent some autonomic or vegetative mechanism in this sphere of physiological activity.

Dr. Clemens E. Benda: It is a great privilege to join in the discussion on the subject of paralysis agitans after the inspiring presentation of Dr. Greenfield. In 1942 Stanley Cobb and I published one of the few pathological studies on paralysis agitans, celebrating at that time the 125th anniversary of James Parkinson's immortal essay on the shaking palsy (1817). The actual neuropathological work was done in 1936, a year before Rolf Hassler (of the Institute of the Vogts) published his study in which the original concept of the Vogts—that paralysis agitans was a disease of the striatum—was revised and the importance of the substantia nigra in all cases of paralysis agitans emphasized.

It is worth while to remember that at the time of our studies it was the undisputed dogma of American neurology that alterations in the substantia nigra were found in postencephalitic Parkinsonism but that paralysis agitans had a different neuropathology and was a disease of the putamen, globus pallidus, and other areas. Our paper established for the first time that cases of paralysis agitans showed severe alterations in the substantia nigra which are well established for the postencephalitic condition. It is a great satisfaction to me to see that after twenty years Dr. Greenfield fully confirms our findings.

As to the so-called "inclusion bodies", we were not certain at that time about the pathological significance and many contemporaries felt they might be artefacts so we did not dare to put any emphasis on this point. It would be a great satisfaction to the late F. H. Lewey, who can be at least partially claimed as a past member of the Boston community through his long association with the Cushing Hospital, to see that the inclusion bodies which he described as early as 1914 have finally found general recognition and are established in their pathological significance, although the nature of the metabolic disorder underlying their formation is still not known.

As Dr. Cobb mentioned in the discussion, we found some evidence in our material of vasoparalytic stagnation of blood flow with unusual enlargement of vessels and perivascular spaces, an observation which had also been emphasized by the Vogts in their term of status cribrosus and re-emphasized by Hassler. I would like to know whether similar observations have been made in Dr. Greenfield's material. These data would be of interest to the clinican because some of the successes of therapy may depend upon achieving a better circulation through the brain.

Dr. Greenfield: Not being a clinician, I cannot answer Dr. Denny-Brown about the nature of the tremor. In reference to his remarks about the inclusion bodies, Lafora pointed out the marked histological distinction between those seen in myoclonus epilepsy and those seen in paralysis agitans. With some staining methods they cannot be confused. There may be some metabolic connection between them, and both may be familial conditions. We are still finding cases of familial progressive myoclonus epilepsy with typical Lafora bodies and we do not find them in paralysis agitans. I am entirely in agreement with him that we are dealing with some metabolic change. I hope that before long we will know more about the metabolism of the nerve cell, and so find a way to stop the progress of the disease.

Dr. Cobb emphasized the distinction between Parkinson's disease and parkinsonism. In general there are many cases in which it is difficult to say whether they are postencephalitic. With a more rapid onset, and in younger people, the disease is more likely to be postencephalitic. In one or two of our cases which came on rapidly, with severe destruction of the substantia nigra, we could not make a distinction. He has also raised the question of the significance of vascular changes in the striatum and cortex. Much of our material was old and it was therefore impossible to use all the staining methods we should have liked, but it was our impression, in going over a large number of basal ganglia, that vascular changes were not greater than those common at the same age. I think Hassler's last paper is important from that point of view. I find it difficult to understand how a perivascular loss of cells can produce such a peculiar range of symptoms. The greater loss of small cells than of large ones, which the Vogts found in paralysis agitans, is described also in chorea. It is difficult to see why one kind of symptom should occur in one disease, and another kind in another disease after the loss of the same cells. The work of Benda and Cobb was important but we were unable to follow it up in any large series because our sections did not include area 6. To make any assessment of the importance of changes in this area would mean a large survey of other areas and this we were not able to do in the time we had.

I am quite unable to answer Dr. Yakovlev's question. I do not know anything about the function of these pigmented cells. One does not consider the pigmented cells to be the only structures involved nor the only ones in which Lewy inclusions may occur. They have been found by many workers, starting with Lewy, in the substantia innominata also. This is another area about the physiology of which we know little and which deserves further study.

I cannot answer Dr. Benda's question about early cases because we had no material of that type.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Meeting of May 19, 1955

DR. ERICH LINDEMANN, President, *presiding*

CENTRAL EFFECTS OF STRYCHNINE ON SPINAL AFFERENT FIBERS.* *J. Y. Lettvin, W. S. McCulloch, W. Pitts, and P. D. Wall,* Research Laboratory of Electronics, Massachusetts Institute of Technology.

First we wished to test some of the many theories on the action of strychnine by testing its effect on the excitability of motor horn cells and of terminal arborizations of spinal afferent fibers. A stimulating microelectrode was placed in the ventral horn of a lumbar spinal segment in anesthetized curarized cats. Recordings were taken of the antidromic volley running in the group one fibers in the dorsal root and of the orthodromic volley running in the segment's ventral root. After intravenous strychnine no change was made in the threshold of the motor horn cells. The terminal arborizations of the afferent fibers showed an increase in threshold. As further evidence for action on primary afferent fibers, it was shown that strychnine affects all components of the electrotonic dorsal root potentials. The earliest components believed to be due only to the passage of impulses in the primary afferent fibers were affected. In these respects, strychine imitates post-tetanic potentiation of reflexes which is due to hyperpolarization of the stimulated fibers. No evidence could be found of a decrease of threshold of the motor-horn cells after strychnine.

Secondly, the nuclei of Goll and Burdach were locally strychninized and recordings were taken from the dorsal columns and lumbar dorsal roots. It was found that synchronized antidromic volleys generated in the strychninized areas ran down the dorsal columns and out of the dorsal roots. The caveats of strychnine neurography were discussed. Five examples are known of strychnine failing to fire off central nerve cells, one example of transynaptic conduction of strychnine "spikes" has been shown in the sympathetic nervous system and above we show antidromic spike propagation in the dorsal columns. So long as such exceptions are considered, strychnine neuronography remains a useful tool as an indicator of organization and as a guide for definitive anaomtical studies.

Discussion

Dr. Paul I. Yakovlev: I should like to ask Dr. Wall what is his understanding of the action of strychnine on the neurone. How does it change the phenomenon of excitability and conduction?

Dr. Wall: We are not suggesting that we have shown the complete action of strychnine. There are two general phenomena one sees in an animal influenced by strychnine: hyperexcitability, and synchronization which may become organised into a tetanus. Strychnine may affect the metabolism so as to increase the polarization across the membrane and produce the hyperexcitability by an increase of the height of the action potential. This is not an adequate explanation of rhythmicity. The question of how a drug increases polarization is beyond the scope of our work.

Dr. J. Y. Lettvin: If you paint a region with strychnine you have all the cells fire off in synchrony. One would expect that they do so because of a common signal to them. This suggests that strychnine activity is initiated in the fibers of termination. The reason the Goll and Burdach experiment was important was because it was the only region where we could be sure no efferent fibers could corrupt the picture down the dorsal columns and out the dorsal roots. We would like to know if there are other regions where input and output are not mixed and accessible.

Dr. Jerome K. Merlis: There are many reports in the literature indicating that after strychnine, cells may show a depression to evoked responses at the same time they are firing strychnine spikes. Do you have any information about the action of strychnine on the synaptic inhibitory arc?

Dr. Wall: Although the work of Eccles shows a decrease of inhibition with strychnine, our own work and that of others indicates that some types of inhibition may be increased. This effect and the possible hyperpolarisation of elements makes it difficult to predict what will happen to the threshold of an evoked response. Fibers are more difficult to fire off when hyperpolarized. Once you can get them to fire off, the result is greater.

Dr. Yakovlev: There is hardly a single fiber system, however compact, that is absolutely a hundred per cent polarized in one direction. It is a matter of density.

Dr. Wall: The evidence for antidromic volleys from the nucleus of Goll was from dorsal roots. I do not know of any evidence for descending fibers which exit from the dorsal roots.

Dr. Yakovlev: In lower forms descending fibers in the dorsal columns are well known. Even in cats and monkeys one would expect some descending fibers from the reticular formation.

Dr. Wall: But the antidromic strychnine spikes which we have shown here not only descend the dorsal columns but also run out of the dorsal roots, whereas the descending fibers which you mention do not exit from the cord and run in the dorsal roots.

FRONTO-MEDIAN LEUCOTOMY FOR PAIN: PSYCHIATRIC OBSERVATIONS ON A PATIENT BEFORE AND AFTER SURGERY. *John C. Nemiah, M.D. and James C. White, M.D.*

A 40 year old male paraplegic underwent a Grantham fronto-median leukotomy for intractable pain

* This work was supported in part by the Signal Corps; the Office of Scientific Research, Air Research and Development Command; and the Office of Naval Research; also, in part, by the Teagle Foundation, The National Science Foundation, and Bell Telephone Laboratories, Incorporated.

in his legs. Pre-operatively, he was agitated and depressed, complaining of pain. In psychiatric interviews he repeatedly responded to questions about his concern over the effect of the injury on his life situation with denial of such concern and complaints of pain. Accordingly, he was interviewed before and after leukotomy and questioned about the effect of paraplegia on his life situation. The interviews were tape-recorded and analyzed for the number of pain and situational responses. There was a marked shift from pain responses preoperatively to situational responses post-operatively (significant at the 0.001 level of probability as tested by Chi Square.) Post-operatively he showed no anxiety nor depression; when questioned, he admitted pain but there was no spontaneous complaint of it. It is postulated that leukotomy physiologically reduced the patient's ability to experience anxiety; as a result the patient could face directly problems around his life situation which had previously created sufficient anxiety to cause a displacement to his pain of conflicts centered around being paraplegic, thereby emotionally increasing his suffering from pain.

Discussion

Dr. Erich Lindemann: This study is notable because it gives us increased rigor on both sides. We are more precise on the lesion of the brain, and we are more precise in appraising the mental status. The use of content analysis of interviews is not as common as it could be. This makes it possible to relate neurophysiological data to some more dynamic aspects. This again is a badly needed exercise.

Dr. Paul I. Yakovlev: This is a most interesting study of a patient with severe physical disability. According to the content analysis preoperatively, there was a great incidence of complaint of pain and distress, anxiety, an accompaniment of distress, and less concern about the meaning of paraplegia. After the operation the concern about the complaint of pain receded into the background, whereas the concern about the meaning of paraplegia connected with livelihood, came more into the foreground. This is somewhat different from the general impression one gets from reports about surgery for pain.

Dr. Nemiah: Before surgery the patient showed a great deal of affect-anxiety and depression. After surgery, there was little, and the patient was apathetic. Before surgery the anxiety and concern were about his pain; when asked a stimulus question about his life situation resulting from the paraplegia, he would appear upset, but deny concern, and complain of pain. After surgery, to the same stimulus question he would talk about his life situation but without affect. In other words, following surgery, there was a diminution of affect, as has been described, *and* a change in the content of his responses to the questions.

Dr. Yakovlev: This presents a rather new point.

Dr. Nemiah: I think we have to distinguish between the concern (the affect) and the content. His concern was not really enhanced after operation; on the contrary, it appeared diminished. With the diminished affect, the content changed in that he talked about the effect on his life of his paraplegia, and not about pain. It was on this basis that we inferred that preoperatively the concern over being paraplegic was displaced to the pain, thus increasing his suffering from it. His talking about the effect of paraplegia postoperatively was not concern.

Dr. Paul B. Jossmann, Boston: The exactness of this new neurosurgical procedure represents a milestone in the history of psychosurgery. The accuracy in placing the lesion and the determination of its size are a safeguard against the previously uncontrollable damaging side effects. Dr. White's observations with repeated operations reopens the discussion of the working mechanism of lobotomies and seems to emphasize the quantitative factor involved.—The reduction of anxiety is an acceptable working hypothesis. Still the question remains what causes the reduction of anxiety physiologically.

Dr. James C. White, Boston: I am sure that the amount of frontal lobe you take off is more important than the area. We have experimented with different methods. In non-psychotic individuals with pain, after the old Freeman and Watts procedure of transecting the entire bundle of white matter on the plane of the coronal suture you get a patient, totally devoid of affect whose social behavior is difficult to say the least. If you transect only the two lower quadrants, you get a patient who is apathetic, but without the bad behavior problems. Then, if you use Scarff's method of complete unilateral leucotomy, you get good relief of pain, provided the patient does not live for more than six months. These patients are not behavior problems, but are not as devoid of psychological abnormalities as Scarff claimed. Dr. Cobb and Dr. Bonner found some degree of apathy, diminution in amount of speech and increase in amount of prodding they had to have to keep them talking. If you do the procedure described tonight, it is something like the bilateral medial lobotomy described by Dr. Solomon. These patients do better than others with the Freeman and Watts operation. You get a minimal change in personality. If these patients had been less physically incapacitated I believe they could have gone back to work and been quite effective.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Meeting of October 27, 1955

Dr. Erich Lindemann, President

This was a clinical meeting at the Boston City Hospital with Dr. D. Denny-Brown presiding. It was felt that since this meeting was clinical in nature, an account of it would be too long for publication.

Schwartz, Leonhard. DIE NEUROSEN UND DIE DYNAMISCHE PSYCHOLOGIE VON PIERRE JANET. (Basle, Switzerland: B. Schwabe & Co., 1951, pp. 455, $8.00.)

This large, handsomely printed and bound book on neuroses and the dynamic psychology of Pierre Janet is by a Swiss neurologist who had made a number of contributions to neurology before he developed an interest in the psychology of patients. Janet, who gave Schwabe his personal library, not only was the latter's close friend but considered Schwartz best qualified to continue his own work. This hope was not fulfilled because Schwabe died in 1948 surviving Janet by less than one year. Janet's scientific publications comprise some 15,000 pages. Hence, the task of reading, digesting, summarizing, and systematizing this vast amount of material was a formidable one, especially since Janet, like most productive writers, changed and improved his ideas during his long lifetime of hard work. Schwabe, who did not live to see his book in printed form performed his task admirably and made a truly noteworthy contribution to psychopathology.

The book has a preface by Robert Bing, with whom Schwartz worked at Basle, and an introduction by Janet himself, giving a good compendium of his fundamental ideas. It is frequently said that Freud started where Janet ended. Actually their systems have very few points in common and hardly any in their basic concepts and principles. Janet, born in 1859, was three years younger than Freud and outlived him by eight years. They were contemporaries. Their main interests and methodologies were so different that their results and conclusions had to be radically different. Janet called his system one of dynamic psychology because he emphasized the potential energy available to patients and the use they made of it. His psychology is dynamic because it deals with human actions. Janet looked in psychopathology for the answers to normal psychology because he assumed, not unlike Freud, that pathological behavior was exaggerated normal behavior. Janet's postulate was that scientific psychology could be created only if all mental phenomena were treated as actions (essential parts of overt conduct, or inhibitory and preparatory phases of activity). Janet's ambition was to build a system of psychology in the manner of a natural scientist, i.e., by first compiling a great many minute observations of objectively verifiable clinical behavior of the patients, and then finding the simplest system of concepts which would allow the vast observational data to be classified in an orderly and simple manner with a minimum of assumptions. Janet started out as a philosopher and logician and received his medical degree only in his 34th year of life after he had published a number of philosophical contributions. He made his most important psychological and psychopathological contributions in his sixties and seventies. They are mainly in the field of descriptive clinical psychiatry. Anyone interested in descriptive clinical psychiatry and in the correlation of psychological traits, verifiable by objective observation, will benefit greatly from a study of this excellent survey of Janet's gigantic published work.

Interested chiefly in precise clinical observations and their systematic classification, Janet limited the scope of his work. His main concepts were amount of available potential energy and management of this energy. Mental illnesses were attributed to various forms of depletion of energy (exhaustion) or to poor energy management. He used the concept of the unconscious but this concept implies only a primitive mental state in which the individual is not reacting mentally to his own activities. It is a state of inefficiency. Consciousness, on the other hand, is described as a higher mental function; it is a proprioceptive reflex, a reaction to one's activities which makes it possible to act with greater efficacy. Voluntary attention intensifies consciousness most and best. Since any voluntary activity requires much effort, it easily leads to exhaustion and brings about unconscious states. According to Janet the term unconscious should be applied only to certain activities which are accessible

to direct clinical observation. Janet's unconscious then is visible while Freud's unconscious is not an observable fact but a logical inference.

The two systems of dynamic psychology are fundamentally different. The main reason for it was the difference in purpose. Janet's ambition was to speculate as little as possible and to build a system of actions out of clinically observable data. Freud was interested mainly in the distant and not directly accessible causes of behavior patterns. This interest led Freud to the invention of his treatment method which was also his chief method of investigating personality. Furthermore, while Janet looked on forgetting, inefficiency, self-injurious behavior as a result of a passive defect state (lowering of mental level), Freud (following Nietzsche) interpreted forgetting as an active process, anxiety as an internalization of conflict between self-centered tendencies and limitations on personal freedom imposed by society for the sake of social order. When the reader realizes the differences in the theoretical and methodological foundations of Janet's and Freud's psychologies, he may reach the conclusion that the two psychological systems need not be mutually exclusive. Janet gave us excellent clinical descriptions of a multitude of psychopathological phenomena, while Freud offered theories designed to explain the etiology of these phenomena. It is probably not a matter of chance that Schwartz was primarily a neurologist. Neurologists are concerned with precise clinical symptoms much more than modern psychiatrists. Thus Janet's system could have a special appeal for Schwartz. Anyone desirous of acquainting himself with Janet's methods and results should consult this outstanding epitome of Janet's life work.

Z. A. PIOTROWSKI

Vedder, Clyde B., Ph.D. THE JUVENILE OFFENDER. (Doubleday and Co., Inc., Garden City, N. Y., p. 510, 1954, $6.00.)

Much has been written and said in recent times on the problem of the juvenile offender. This book is in the form of a prospectus, bringing together in one volume a diversity of articles on the subject. Each chapter consists of a succinct, often revealing, survey of the topic which is followed by pertinent collected readings. The basic approach to delinquency presented here is from the sociological standpoint, although the offender is studied as an individual in certain chapters. The majority of contributions are by leading sociologists, educators, public authorities, judges, social workers, welfare workers, and a few by physicians and psychiatrists. The author expresses the hope that this work will further greater cooperation and understanding of this complex problem.

The presentation, notably wide in its scope, gives first consideration to defining the subject matter, the extent and significance of the problem, and etiological factors. The role of community organization, such as church and school, is presented. One chapter is devoted to the significance of individual personality problems. Of special interest is the material on the origin, structure and function of juvenile gangs. Considerable attention is paid to the problems entailed in coping with delinquency, with detection of offenders, and the role of the juvenile court, probation and correctional institutions in remedying the problem. Here the inadequacies of the courts, lack of personnel, and defective attitudes are strikingly revealed. The severity of the problem and failure in correction is convincingly shown by the figures showing between 65% to 85% rehabilitative failures among former inmates of correctional institutions. The author justly asks: "Does the correctional institution correct?" The final chapter emphasizes that this problem is a community responsibility and any effective remedial effort must begin on the local scene and with the coordinated efforts of all community resources and groups.

The book is a supplement to a text and will be of particular value to students of sociology. However, it has much to offer social workers, psychiatrists, educators, and all those actively participating in coping with juvenile delinquency.

FRANCIS J. BRACELAND

Bosselman, Beulah Chamberlain. THE TROUBLED MIND. (New York: The Ronald Press Company, 1953, pp. iv + 206, $3.50.)

Dr. Bosselman, a practicing psychiatrist and psychoanalyst, and a contributor to professional journals, offers, in *The Troubled Mind*,

a book of distinct worth. Although she has aimed her discussion toward the non-professional reader, she has wisely and capably avoided any appearance of "talking down" to some pre-supposed level. On the other hand, neither does she take refuge in technical terminology which might be unintelligible to the average reader. Instead, she maintains throughout a conversational tone which is extremely effective in aiding her to achieve her goal of explaining personality development and personality disorders to the layman.

As would be expected, the author's orientation is psychoanalytic, and some psychoanalytic concepts are necessarily utilized. These, it may safely be said, are kept to a minimum, and it is highly improbable that those of other orientations would find much to disapprove. Dr. Bosselman develops her topic by analyzing concisely the processes of human development, emphasizing those specific problems which must be solved at each age level from infancy through old age, if one is to attain a satisfactory state of adult adaptation. Having established this foundation, she discusses the end products of adaptive processes which have failed, the neuroses and psychoses. The latter third of the book is entitled "The Problem of Treatment" and in it, she considers the various agencies and disciplines concerned with treatment, their backgrounds, and their functions. A bibliography, "Suggestions for Further Reading", is appended. It seems likely that the average reader will need some degree of guidance in making selections from this list, inasmuch as an extremely wide range of material is included. For example, under the general heading "Psychiatry and Psychoanalysis: Aims and Techniques", two of the nineteen items listed are Alexander and French's *Psychoanalytic Therapy* and Menninger and Leaf's *You and Psychiatry*.

This book will be found of value by those physicians and other professional people who are asked to recommend readings in the area of mental health. It certainly will be well received by those to whom it is recommended, and reasonably careful reading of it should furnish a basis for greater understanding and for further discussion with the physician.

BARTON W. KNAPP

BOOKS RECEIVED FOR REVIEW

July, 1955

1. CLECKLEY, H. The Mask of Sanity. The C. V. Mosby Company, St. Louis, Missouri.
2. DIETHELM, O. (Ed.) Etiology of Chronic Alcoholism. Charles C Thomas, Publisher, Springfield, Illinois.
3. DIETHELM, O. Third Edition: Treatment of Psychiatry. Charles C Thomas, Publisher, Springfield, Illinois.
4. LAFFONT, A. (Director) Encyclopedie Medico-Chirurgicale (3 books). Editions Techniques S. A., Encyclopedie Medico-Chirurgicale, Paris, France.
5. MASSERMAN, J. H. The Practice of Dynamic Psychiatry. W. B. Saunders Co., Philadelphia, Pennsylvania.
6. Muscular Dystrophy Association of America, Inc. Proceedings of the Third Medical Conference of Muscular Dystrophy Association of America, Inc., October 8 and 9, 1954. Muscular Dystrophy Association of America, Inc., New York, New York.
7. Veterans Administration. Veterans Administration Technical Bulletins, Series 10. Veterans Administration, Department of Medicine and Surgery, Washington 25, D. C.

NOTES AND NEWS

VETERANS ADMINISTRATION ADVISORY COMMITTEE IN RESEARCH

Appointment of an Advisory Committee on Research to counsel the Chief Medical Director concerning research programs conducted within Veterans Administration has been announced by Dr. William S. Middleton, Chief Medical Director.

The committee is composed of representatives of specialists in internal medicine, surgery, neuropsychiatry, and tuberculosis. The chairman is Dr. Joseph M. Hayman, Dean of Tufts College Medical School in Boston.

The four members are:

Dr. J. Burns Amberson, consultant to the Chest Service of Bellevue Hospital in New York City.

Dr. Carol A. Moyer, Professor of Surgery at the Washington University School of Medicine in St. Louis.

Dr. W. Reece Berryhill, Dean of the University of North Carolina School of Medicine at Chapel Hill; and

Dr. Harold G. Wolff, Associate Professor of Psychiatry at Cornell University Medical College in New York City.

The specific aims of the committee are to assist in developing and maintaining desirable research programs within VA.

These aims are to be achieved through periodic review of the objectives, plans and activities of the research program and through an evaluation of research activities, including their administration and accomplishments.

The committee may advise the Chief Medical Director and the Assistant Chief Medical Director for Research and Education through recommendations regarding their research activities, including their planning and conduct. It also will report such findings and recommendations as it deems desirable to the Special Medical Advisory Group.

The committee will be concerned particularly with the professional and administrative aspects of the research activities conducted within VA stations and with the research activities conducted by VA employes, and also to their interpretation to the lay public as well as to individuals with professional, scientific, and technical interests.

This committee will maintain contact with the Committee on Veterans Medical Problems of the National Research Council which has advised VA on matters of research since it was established in 1945.

NATIONAL MENTAL HEALTH GRANTS

The National Institute of Mental Health, Public Health Service, U. S. Department of Health, Education, and Welfare announces *December 15, 1955* as the closing date for the year beginning July 1, 1956 for filing applications for grants under the National Mental Health Act in support of training programs in psychiatry, clinical psychology, psychiatric social work, and psychiatric nursing. Applications may also be made by university training centers for the support of career teacher programs for the preparation of teaching personnel in the mental health disciplines.

The deadline date for filing applications for the support of pilot and evaluation studies proposing new method of teaching, or evaluation of teaching and training methods in the mental health disciplines, is *January 15, 1956*.

Application forms and details regarding the types of support available may be obtained from the Chief, Training and Standards Branch, National Institute of Mental Health, National Institutes of Health, Bethesda 14, Maryland.

WESTERN REGIONAL RESEARCH SYMPOSIUM

In cooperation with the American Psychiatric Association, the Department of Psychiatry of the U.C.L.A. Medical School and University of California Extension have announced plans for a two-day Western Regional Research symposium on the "Application of Basic Science Techniques to Psychiatric Research", to be held in Los Angeles in January.

Norman Q. Brill, M.D., Donald B. Lindsley, Ph.D. and Charles W. Tidd, M.D. head a planning committee for the program on

January 26 and 27. Throughout the two day symposium sessions will be held in room 2147 of the U.C.L.A. Life Sciences Building.

The course is open to psychiatrists, psychologists, psychiatric social workers, psychiatric nurses and others with the consent of the course chairman, according to Thomas H. Sternberg, M.D., assistant Dean for Postgraduate Medical Education at U.C.L.A. The conference will convene at 9:30 on the first morning with U.C.L.A. Chancellor Raymond B. Allen, M.D., Stafford L. Warren, M.D., Dean of the School of Medicine, and Dr. Sternberg making the welcoming remarks. During ensuing sessions topics will include Brain Mechanisms and Behavior, Experimental Studies of Psychosomatic Disease, Methods of Blocking Neuroendocrine Mechanisms, Brain Metabolism and numerous related subjects.

Requests for information and registration blanks should be addressed to Dr. Thomas H. Sternberg, University of California School of Medicine, Los Angeles 24, California. Fee for the symposium is $3.50 made payable to the Regents of the University of California.

POSITIONS FOR PSYCHOLOGISTS

A civil service examination has been announced for Counseling Psychologist (Vocational) for filling positions paying from $6,390 to $10,320 a year in Veterans Administration hospitals and centers throughout the United States, and in the Department of Medicine and Surgery of the Veterans Administration in Washington, D. C.

No written test is required. To qualify, applicants must have completed all the requirements for the doctoral degree with major emphasis in the field of psychology and, in addition, have had appropriate experience.

Applications will be accepted until further notice by the Executive Secretary, Central Board of U. S. Civil Service Examiners, Veterans Administration, Washington 25, D. C.

Further information may be obtained from many post offices throughout the country or from the U. S. Civil Service Commission, Washington 25, D. C.

THE MENNINGER FOUNDATION INITIATES AN EXPERIMENTAL TRAINING PROGRAM IN ADMINISTRATIVE PSYCHIATRY

An experimental training program in psychiatric hospital administration has been initiated at The Menninger Foundation, Topeka, Kansas, with cooperation from Winter Veterans Administration Hospital and Topeka State Hospital. First trainees in the project are Doctor Robert Allen Haines, on leave as superintendent of Apple Creek, Ohio, State Hospital, and Doctor George Zubowicz, formerly director of allied clinical services at Topeka State Hospital.

The program is the first to provide a one-year formal training period required by the American Psychiatric Association which in 1953 issued standards for examining and certifying medical hospital administrators. APA has granted temporary approval to the program for a period of two years, after which it will be reviewed.

Doctor R. C. Anderson, manager of Winter VA Hospital is director of the program and assistant director is John R. Malban, formerly business administrator at Logansport, Indiana, State Hospital.

Physicians wishing further information about the program and application procedures may obtain it by writing Malban at The Menninger Foundation, Topeka, Kansas.

RESEARCH FUND FOR MULTIPLE SCLEROSIS

The Multiple Sclerosis Foundation of America has presented $25,000 to Northwestern University medical school for research on the disease. The funds will be used to support research in progress as a team project among five departments at the school.

Dr. Lewis J. Pollock, emeritus professor and chairman of the department of neurology and psychiatry, is in charge of the program. Phases of the studies are being done in the department of biochemistry by Dr. Smith Freeman, professor and chairman of the department, Dr. Norman Radin, assistant professor, and Dr. E. A. Zeller, professor.

Other research is being carried on by Dr.

Harry B. Harding, associate professor of bacteriology, by Dr. William Wartman, professor and chairman of the department of pathology, and by Dr. Derrick Vail, professor and chairman of the department of ophthalmology.

Multiple sclerosis is a crippling disease of the nervous system. More than 300,000 Americans now have it. The cause is not known and there is no known cure.

The Multiple Sclerosis Foundation of America has given $125,000 to Northwestern University in the past five years for studies that might yield information toward finding the cause of the disease or a treatment for it.

Attempts are being made to isolate and identify any infectious agent that might be the cause of multiple sclerosis and attempts are being made to cultivate central nervous system cells in chick embryos for the purpose of trying to infect them from multiple sclerosis patients.

Sensitive tests devised at the medical school for the determination of small amounts of enzymes in the spinal fluid are being used to determine if enzymes play a role in causing the disease. Biochemical and histologic studies are being done on the body fluids and tissues of multiple sclerosis patients and patients without multiple sclerosis to try to find differences to point to possible mechanisms involved in the disease.

Various drugs are being tested for the treatment of multiple sclerosis and the manifestations of the disease in the eyes are being studied.

NORTH SHORE HEALTH RESORT LECTURES

The fourth lecture in the Sixth Annual North Shore Health Resort Lecture Series on *Psychiatric Problems in Medical Practice* will be held on Wednesday evening, January 4, 1956 at 8:00 p.m. at our hospital 225 Sheridan Road in Winnetka, Illinois.

The Management of the Depressed Patient will be discussed by Franklin G. Ebaugh, M.D., Clin. Prof. of Psychiatry, U. of Colorado School of Medicine; Regional V.A. Cons.; Member Res. Review Com. of A.M.A.; Editorial Board of many professional journals, Denver.

The fifth lecture in the Sixth Annual North Shore Health Resort Lecture Series on *Psychiatric Problems in Medical Practice* will be held on Wednesday evening, February 1, 1956 at 8:00 p.m. at our hospital, 225 Sheridan Road in Winnetka, Illinois.

The Management of Emotional Practices in the Male Involutional Period will be discussed by Otto Billig, M.D., Associate Professor of Psychiatry, Vanderbilt University School of Medicine; Psychiatrist-in-Chief, Outpatient Department, Vanderbilt University Hospital, Nashville.

EXPANSION OF RESEARCH IN MENTAL DEFICIENCY

The Research Department of Letchworth Village, Thiells, New York, one of the oldest centers for the study of mental deficiency has been recently expanded. The New York State Department of Mental Hygiene has granted additional funds and a section on biochemistry has been added in charge of Fred B. Goldstein, Ph.D., who will study abnormal metabolisms in certain types of mental deficiency.

ASSOCIATE PROFESSOR OF PSYCHIATRY APPOINTED AT CHICAGO

Appointment of Dr. H. Waldo Bird, Detroit psychiatrist and former faculty member of Wayne University, as associate professor of psychiatry in the University of Chicago School of Medicine has been announced by Dr. Lowell T. Coggeshall, dean of the University's Division of Biological Sciences.

In private practice in Detroit since 1949, Dr. Bird also held a clinical appointment in the College of Medicine, Wayne University. In 1949–50, he was psychiatrist and acting director of the Adult Psychiatric Clinic in Detroit.

Dr. Bird was active in the formation of the Michigan Association for Epilepsy, serving as chairman of the organizational development committee, and was also psychiatric consultant and chairman of the research committee of the Michigan Epilepsy Center.

Dr. Bird has also served as chairman of the Committee of Mental Health of the Michigan State Medical Society and chairman of the

Committee on Standards, Practices and Facilities of the Michigan Society of Neurology and Psychiatry.

A NEW MAGAZINE: NEURO-CHIRURGIE

Masson et C^ie^ Editeurs, 120 Boulevard Saint-Germain, Paris

As a result of the expansion of neuro-surgery and of the technical means made available to it, this branch of the medical science is gradually distinguishing itself from the others, having its own techniques, its own specialists and its own teaching. This expansion made it necessary to issue a periodical in the French language intended only for this new specialized branch.

The first number of *Neuro-Chirurgie* appeared in February 1955. This review is essentially designed to spread the works and the discussions of the members of the French speaking Neuro-Surgery Society. But, the greater part of it is devoted to the publishing of original dissertations in the French language, selected among the communications brought before the society, or submitted by foreign authors to the society. These dissertations and communications will be contained in four issues yearly.

NEW PSYCHIATRIC JOURNAL

The first two numbers of Volume I of the *International Journal of Social Psychiatry* (the New Quarterly of Interdisciplinary Research) have been published by the Avenue Publishing Co., 9 Fellows Road, London, N.W. 3, with Dr. Joshua Bierer of London and Dr. Thomas A. C. Rennie of New York as chief editors. The first number serves as an excellent orientation in this important field. The article entitled Social Psychiatry—A Definition by Dr. Rennie gives one the facts, the scope, and the issues involved. We predict a successful career for this new journal.

ERRATUM

In an article in an earlier issue of this JOURNAL (1), the following statement is made: "In another paper (11) Levy and Kennard have considered high alpha index, as well as low voltage fast activity, to be abnormal!" This is an error, and is hereby corrected with apologies to Levy and Kennard. The reference is to a 1953 paper (2), in which Levy and Kennard, on page 426, discuss high alpha index and low voltage fast activity, together with theta, fast abnormality, and paroxysmal features, and table these phenomena under the heading "Significant EEG Characteristics." They do not state nor imply that all of these characteristics are abnormal. This error is entirely the fault of the undersigned, and not that of Dr. Sisson.

ROBERT J. ELLINGSON

(1) Sisson, B. D., and Ellingson, R. J.: On the relationship between "normal" EEG patterns and personality variables. *Journal Nervous & Mental Disease, 121:* 353, 1955.

(2) Levy, S., and Kennard, M. A.: The EEG Pattern of patients with psychological disorders of various ages. *Journal Nervous & Mental Disease, 118:* 416, 1953.